Medical Library

SEP 21 1942

VOL. IV. No. 3 JULY, 1942

BRITISH HEART JOURNAL

EDITORS
MAURICE CAMPBELL
D. EVAN BEDFORD

APPOINTED BY
THE CARDIAC SOCIETY OF GREAT BRITAIN AND IRELAND

CONTENTS

PAGE

A Curious Syndrome, with signs suggesting Cervical Arterio-venous Fistula, and the Palses of Neck and Arms lost. By THOMAS LEWIS and JOAN STOKES 57

The Conducting System of the Vertebrate Heart. By FRANCIS DAVIS 66

The Sino-Auricular Node: A Historical Note. By ARTHUR KEITH . 77

Chest Leads in Congenital and Acquired Dextrocardia. By J. S. RICHARDSON 80

Electrocardiographic Changes due to Trauma. By HUGH BARBER . 83

Electrocardiogram in Friedreich Disease. By WILLIAM EVANS and GORDON WRIGHT 91

Intracardiac Tumours. By J. L. HAMILTON-PATERSON and L. I. M. CASTLEDEN 103

Graham Steell. By CRICHTON BRAMWELL 115

LONDON
BRITISH MEDICAL ASSOCIATION
TAVISTOCK SQUARE, W.C.1

PUBLISHED QUARTERLY SUBSCRIPTION 25/- PER ANNUM. U.S.A. $6.00

EDITORIAL BOARD

APPOINTED BY
THE CARDIAC SOCIETY OF GREAT BRITAIN AND IRELAND

CRIGHTON BRAMWELL, MANCHESTER
BOYD CAMPBELL, BELFAST
JOHN COWAN, GLASGOW
FRANCIS R. FRASER, LONDON
A. G. GIBSON, OXFORD
JOHN HAY, LIVERPOOL
SIR THOMAS LEWIS, LONDON
HENRY MOORE, DUBLIN
JOHN PARKINSON, LONDON
W. T. RITCHIE, EDINBURGH
K. D. WILKINSON, BIRMINGHAM
EDITOR OF BRITISH MEDICAL JOURNAL

NOTICE TO CONTRIBUTORS

Contributors, who do not know the Editor's present address, should send papers to:

Maurice Campbell,
B.M.A. House,
Tavistock Square,
London, W.C.1.

Papers dealing with problems of the heart or of the circulation are accepted on the understanding that they have not been and will not be published in whole or in part in any other journal.

Papers sent for publication must be typed as concisely as possible with double line spacing and a good margin. They must be accompanied by a short summary. Manuscripts should be carefully revised as alterations in print are costly and apart from slight corrections will be charged to the contributor. The author whose name comes first will receive one proof in page.

Illustrations must be ready for reproduction, except that on figures lettering which is written in pencil will be replaced by printer's type without charge. The lettering on electrocardiograms should be done in ink and they should be mounted ready for reproduction.

Where there are many electrocardiograms, only a few complexes should be shown, so that several can be mounted together, and their total width should not exceed $4\frac{1}{2}$ inches, or at the most 5 inches.

References to papers in the text should be made by the name of the author and the year, with or without brackets. At the end of the paper they should be arranged alphabetically as below, according to the Harvard system.

Author's name, Initials, Year, Journal (abbreviated according to the World List of Scientific Periodicals), Volume number, Page number, *e.g.*,

Cowan, J. (1929). *Quart. J. Med.*, 22, 237.

Fifty reprints will be given to the author or divided among the authors on giving notice when the proof is returned. Further reprints, if desired, may be obtained from the Secretary of the Journal Board, B.M.A. House, Tavistock Square, London, W.C.1, to whom all business communications should be addressed.

The subscription, 25/- per annum (20/- to members of the B.M.A.), is payable to the British Medical Association. Applications for advertisement space should be made to the Advertisement Manager, B.M.A. House, Tavistock Square, London, W.C.1.

A CURIOUS SYNDROME, WITH SIGNS SUGGESTING CERVICAL ARTERIO-VENOUS FISTULA, AND THE PULSES OF NECK AND ARMS LOST

BY

THOMAS LEWIS AND JOAN STOKES

From the Department of Clinical Research, University College Hospital Medical School

Received March 24, 1942

A married woman of 33 years was admitted to hospital on November 25, 1941, complaining of attacks of faintness. She is said to have been rickéty as a child and was not allowed to swim at school. After growing up she attended hospital for deafness of her left ear. A doctor examining her in her twenty-sixth year found no pulse at the wrist.

She states that her fainting attacks have been present for about six years and that recently they have become more frequent and now occur almost daily. In the attack her vision becomes dim, she feels weak and would fall without support, but she does not believe she loses consciousness. Her tongue has never been bitten nor her water passed in the attacks. They occur while she is up and about, and also when she is in bed, but especially when she sits up in bed. They are usually followed by headache. She has dropped things from her hand while carrying them, and has collapsed and fallen in the street, but has never hurt herself.

Headaches have been frequent recently; they are severe and felt over the top of the head. She lost the sight of her right eye two years ago in one of her attacks. When scrubbing or doing other hard work she has to stop from time to time owing to aching pain in her arm. Her fingers sometimes become numb and cold without apparent reason.

She has had no children; a pregnancy nine months ago was terminated.

Condition.—She is a small, thin woman (weight, 6 st. 5 oz.). No abnormalities are found in her nervous system, except nerve deafness in the right ear, and a primary optic atrophy in the fundus of the right eye; the vessels of the fundus are normal and there is no exudate. The face is warm and pale and the hands are usually warm and of good colour. Her temperature is usually subnormal; the heart rate varies between 75 and 100 a minute while she lies in bed. Her respirations are 20–24 a minute. The Wassermann and Kahn reactions are repeatedly negative. The blood count is normal. X-rays show no defect in the optic foramina, but the clinoid processes (anterior and posterior) on the right side are eroded.

Heart.—The venous pressure and the venous pulse are normal. The

heart is not enlarged to percussion; the impulse is in the fifth space, 10 cm. from the midline. The sounds are clearly struck and the action regular. The X-ray silhouette, including the arch of the aorta, is normal in outline, but the aortic shadow and that of the basal vessels is rather dense. There is no tracheal tug. The electrocardiogram is normal in its initial phases in all leads.

Arteries and blood pressure.—No pulse can be felt in any artery of either arm, head, or neck. In the neck the pulseless carotid arteries can be felt as unusually firm smooth round cords throughout their length. The innominate vessel can be felt crossing the trachea in the episternal notch; it pulsates palpably though not strongly and is continued into the pulseless carotid vessel. The Pachon oscillometer gives no movement from the upper arms, but the brachial arteries are easily felt as unusually firm round cords throughout their length. The abdominal aorta pulsates freely, the femoral pulses are powerful, and the pulses of the feet are easily palpable, but not waterhammer in quality.

The blood pressure in the popliteal artery, read on a number of occasions, is 210–230 systolic (readings of two years ago were similar) and 130 diastolic. In the arm, blood pressure is obtained by holding the arm aloft for a moment and occluding all circulation by means of the pressure cuff; and then, after an interval of three minutes, allowing the pressure to fall in steps until the hand flushes. Sharp readings can be obtained in this way, showing the mean pressure to be 45 to 55 mm. It can also be shown that the brachial arteries are carrying blood; for if, when the circulation to the limb has been occluded, the brachial artery is firmly gripped and the pressure in the cuff then deflated, reactive hyperæmia is delayed until the brachial artery is released, say fifteen or twenty seconds later, while the hyperæmia occurs in two or three seconds if the brachial artery has not been held. Similarly it can be shown that the subclavian artery is carrying blood; for if the artery is held below the clavicle the colour begins to return only slowly to the hand in five seconds and is full at ten seconds; whereas it returns almost at once if the subclavian artery is free. Compression of the left carotid artery, but not the right, is usually followed by an attack of faintness and pallor, with flushing of the face on release.

Just above the right sternoclavicular joint a systolic thrill and a continuous murmur, louder in systole, are conspicuous. The murmur is heard maximally at the black circle of the diagram, but extends over the whole sternal, supra-clavicular, and supracapular regions (cross-hatched area). The systolic thrill is synchronous with the innominate impulse. No unusual pulsation is to be felt in this region. The veins of the neck are inconspicuous and undistended while the patient lies recumbent.

Anastomotic arteries.—A systolic murmur is heard over large areas of the chest and abdominal wall (the hatched areas of the chart). The areas of the systolic murmur are similar to those heard over the anastomotic vessels in coarctation of the aorta, as previously reported (Lewis, 1933). In the present case arterial pulsations are also to be felt in several places on the abdominal wall; one conspicuous pulsation is present to the right of the navel and the systolic murmur is loud here. A faint pulse has been felt at one or two points

on the back of the chest too, and a systolic murmur is audible at the angle of the right scapula. It seems clear that the chief anastomoses unite arteries of the neck and sternal regions, and with especial freedom on the right side, through the epigastric and internal mammary arteries. An indication of the direction of flow in the main anastomotic arteries is obtained by timing the

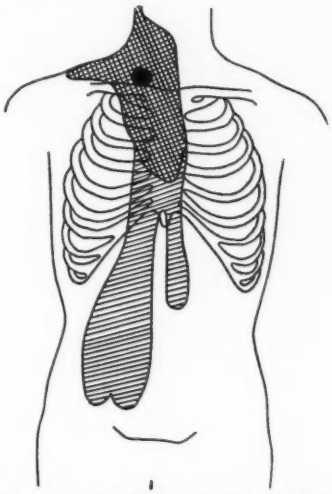


FIG. 1.—Case 1. The area where the systolic murmur could be heard is hatched and the area of the continuous murmur is cross-hatched. The maximal point of thrill is marked by the black circle above the clavicle.

pulsations graphically. The innominate pulse precedes the femoral at Poupart's ligament by about 0·1 sec.; the pulsations of an anastomotic artery near the navel precedes that of the femoral by a little less than this value. Thus the order is innominate, abdominal wall, femoral; closure of the common femoral artery is without effect on pulsations in the abdominal wall. The third and fourth ribs present a few small but unusual crenations of their lower borders.

Renal functions.—The urine is of normal quantity and specific gravity and contains no abnormal constituent. The urea concentration test gives a value as high as 3·09; the urea clearance is 70 per cent of normal, and the blood urea 30 mg. per 100 c.c.

The attacks.—A number of the attacks have been witnessed by her husband, by nursing staff, and by patients in adjoining beds. These attacks are brief, lasting usually ten to twenty seconds, and once about two minutes. Pallor with subsequent cyanosis and noisy breathing are usually noticed. Rigidity, with head retraction, is usual, and unconsciousness not infrequent. Sometimes in the attacks movements of rotation occur in the forearms. In one attack the heart accelerated to 144 a minute, and the patient complained subsequently that her whole right arm had become paralysed for a few moments. Attacks have been provoked by sitting up or kneeling up in bed and leaning over her locker; but the patient always has time to resume the supine position.

Discussion

The patient described presented signs of a very unusual vascular anomaly. No pulsation could be found in either of the carotid or subclavian arteries; the mean blood pressure in the arms was only 50 mm.; and the arms readily developed the ache of muscular ischæmia when used. The patient suffered from frequent attacks of faintness or transient loss of consciousness, and from a unilateral optic atrophy of a few years standing. These evidences all point to a grossly deficient circulation to the head and neck and to the two upper limbs.

The establishment of a great difference between the pressures in upper and lower parts of the body in such a case as this has a clear physiological basis; the low pressure in the upper parts, and presumably in the carotid regions especially, will call forth persistent vasoconstriction, and this will raise the pressure in the lower parts. It is here to be noted that no direct explanation other than the physiological could be found in our patient to explain the raised blood pressure. High pressure in the legs has been recorded in cases of aneurysm with pulseless upper parts by Maurer (1939), Kampmeier and Neumann (1930), and Cohen and Davie (1933). Thus our case in following physiological expectation appears to conform to a rule.*

The aorta itself was unchanged in form and size, its ascending and transverse parts being clearly visible in the X-ray, and the pulse being transmitted without undue delay to the femoral arteries. A pulsation, promptly delivered from the heart, was readily felt in an artery that was regarded from its size and position as the innominate, at the root of the neck; this vessel could be traced upwards into the firm non-pulsating cord of the right carotid. The deficient circulation to the upper parts of the body was manifestly due to an impervious condition, relative or absolute, of subclavian and carotid arteries on both sides.

In most of the instances of lack of pulsation in both carotids and subclavians previously recorded, the patients have been proved to be syphilitic, and those coming to post-mortem examination have been cases of aneurysm of the aorta, the obstruction being due to clot extending into and plugging the mouths of the arteries arising from the arch of the aorta, or to closure of these mouths by sclerosis. Such an explanation is not open to us in the case of a young woman, giving repeatedly negative Wassermann and Kahn reactions,

* Such conformity re-emphasizes the curious blood pressure picture in cases of coarctation of the aorta. The condition as a whole might be likened to one of inverted coarctation of the aorta in its effects on the general pressures. Giffin and Dill have already drawn this analogy in the description of a not dissimilar case.

In 1933 the blood pressure readings from previously recorded cases of coarctation of the aorta were collected for the first time, and to these were added those from eight newly recorded cases (Lewis, 1933). From this material it was possible to conclude that high blood pressure in the upper parts of the body is the rule in these cases, while low pressure prevails in the lower parts. It could not be overlooked that the high pressure in the upper half of the body might be due to a mechanism set in motion by the need of the lower part of the body, but, when examined, the nature of this mechanism remained, and still remains, obscure. Goldblatt, Kahn, and Hanzal (1939) have since shown that clamping the abdominal aorta just above the renal arteries causes a delayed hypertension to develop, as a result of renal ischæmia. Possibly a similar mechanism applies to coarctation, though the freedom of anastomoses and the infrequency of renal insufficiency in these cases is to be noted.

and presenting under X-ray no trace of aortic dilatation or distortion. Giffin (1939) in describing a case very similar to the present one, a woman of 19 years, was for similar reasons precluded from assigning it to syphilis; and consequently in the discussion of his case, a congenital anomaly of arteries was suggested as the possible basis of the lesion. It is but a suggestion, for no such anomaly is known in which all of the three usual vessels, innominate, subclavian, and carotid, fail; or which would account for loss of pulses in head, neck, and arms. We may place the argument on more general lines. When a usual artery, such as those named, fails to arise from its accustomed parent stem, it arises from some other source. *The congenital anomalies of arteries are not suppressions of arterial supply, they are merely unusual arrangements of supply.* In thinking of a developmental failure of arterial supply, it is to be remembered that the first arrangement of main arterial paths is determined at an early stage of uterine life, at a time when the limbs have still to make the great bulk of their growth. That adequate arterial development should fail while the tissues and structures of the corresponding territory continue to develop normally from this early stage is inconceivable. The evidence from our patient is of a gross defect of circulation to the head and limbs. To account for this state an anomaly of development would be, by itself, an inadequate explanation.*

It would seem necessary to adopt an explanation embracing an acquired lesion. The nature of the acquired lesion remains obscure; a chief clue to it being the remarkable cord-like condition of the main arteries in the neck and arms, already described. Extensive thrombosis might be expected to have produced at the time sudden and emphatic cerebral symptoms; it might also be expected to have rendered the vessels concerned quite impervious; yet as we have seen the brachial arteries and probably the left carotid, though greatly thickened, were not impervious. A dissecting aneurysm spreading to the basal vessels is a possible explanation, but there is no definite support for the suggestion.

In searching for an interpretation of this curious case there is another feature which stands out and calls for explanation, namely, the continuous murmur and thrill at the base of the neck. It is such a murmur and thrill as is known to occur only where a main artery is in communication with another vessel under much lower tension. Simple anastomoses are not known to give continuous murmurs. Although an arteriovenous fistula is the most probable explanation, yet it may be objected that increased pressure in the veins of the neck, and a steep-rising pulse in the legs, would be expected in association; neither of these phenomena occurred. Such a fistula can by no means be excluded, however, since it may have been deeply seated, as in the bones of the vertebræ or skull; no evidence in support could be found in X-ray pictures of the neck, though the sella turcica was seen to be malformed, the clinoid

* Coarctation of the aorta cannot legitimately be cited in the contrary sense, for this defect is not supposed to occur by failure of development, but by some form of interference, at or about the time of birth, causing the already open aorta to close down in the region of insertion of the ductus arteriosus.

processes being small and obscure. No murmur could be heard over the head. The anastomosing vessels in the case are more consistent with the idea of an arterio-venous fistula than with that of a purely obstructive lesion necessitating collateral supply of the head and arms from the lower parts of the body. As has been seen, the collateral channels did not lead upwards through epigastric and internal mammary from femoral to supraclavicular region.

A point upon which considerable emphasis is to be laid is that Giffin's case, so like ours in other respects, also presented a continuous thrill in a similar situation. So did a patient whom we saw many years ago. This was a young woman, the pulse in whose neck was absent or almost imperceptible. The Wassermann reaction was negative, but the aorta was definitely dilated. This case is of special interest in that the blindness was known to have resulted from a recent obstruction of the central artery of the retina. The notes of this case, imperfect though they are, and an abstract of Giffin's case are appended. Here then are three cases of very similar type, and all presenting a similar murmur. The fact suggests that we are dealing with a pathological entity hitherto unrecognized and still awaiting post-mortem dissection before its precise form can be understood.

Appended Notes of Another Case

Case 2. A housewife of 45 years was admitted to hospital in the autumn of 1932, complaining of attacks of faintness, and blindness of the right eye. She also suffered at this time from bronchitis. There was a history of rheumatic fever at 8 years and of white leg and varicose ulcers following pregnancy. She was the mother of seven children, five alive and well. One child came prematurely and died, and one died at fourteen months from rickets and pneumonia.

In March 1931, when in hospital for pregnancy, it was found that pulsation in her radial and carotid arteries was much diminished; this was the first record of any abnormality of her vascular system. The fainting attacks began during pregnancy in 1930 and occurred about once in five weeks; they were usually provoked by sitting up in bed in the morning and were also brought on by stooping. They comprised mistiness of vision, dizziness, and weakness in the left arm, followed by numbness and tingling and often by severe headache. Consciousness was not lost. The blindness came suddenly during an attack of " influenza."

Condition.—She was a healthy-looking and well-nourished woman (weight, 11 st. 5 lb.). Her colour was good and her hands and face warm. Her temperature was usually subnormal and her heart rate varied while she was in bed from 68–84 a minute. There were no abnormal signs in her central nervous system and the loss of vision in the right eye was stated by Mr. H. Neame to arise out of recent obstruction of the retinal artery. The retina was pale and œdematous, especially at the macula, which presented a bright red spot; the arteries were very thin and of irregular lumen, the veins smaller than normal;

the œdema subsided subsequently. Her Wasserman reaction was found negative on two occasions.

Heart.—Venous pulsation and pressure in the neck were normal, and the heart was not enlarged. Some retrosternal dulness and pulsation could be seen in the third right space during full expiration. There was no pulsation of the sternum and no tracheal tug. X-ray of the chest confirmed that the

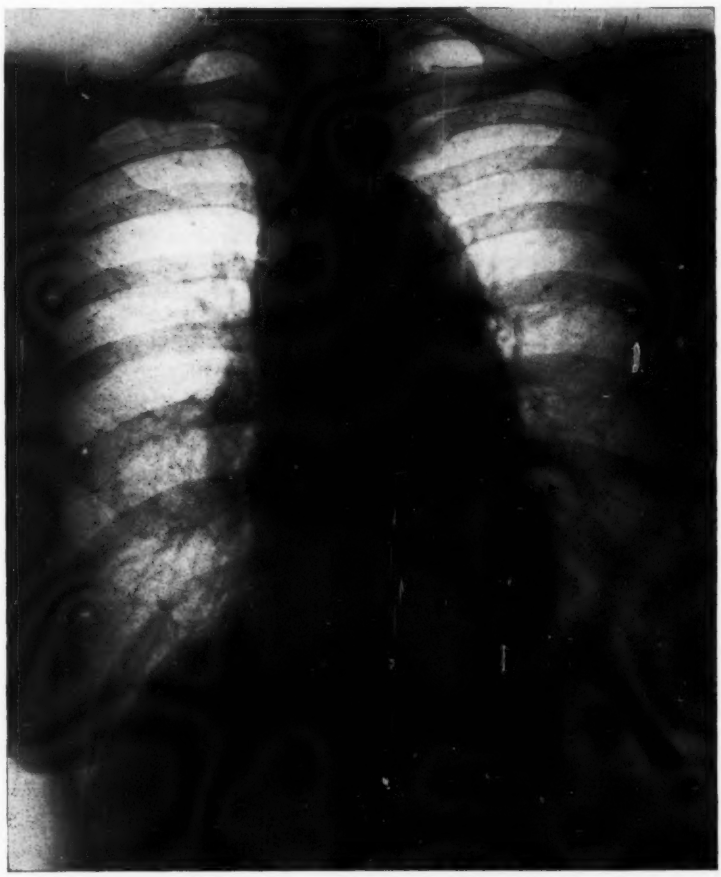


FIG. 2.—Case 2. Antero-posterior radiogram of the chest, taken on October 12, 1932.

heart was normal in size and showed a diffuse dilatation of the aortic arch and a shadow running from the arch of the aorta, parallel to the right border of the sternum to the region of the sterno-clavicular joint, presumably a dilated innominate vessel (see Fig. 2). There was no notching of the ribs such as is seen in cases of coarctation of the aorta. The electrocardiogram was normal.

Arteries and blood pressure.—In the right radial artery only a flicker of pulsation could be felt. The right brachial and carotid, and the left radial, brachial, and carotid arteries were not felt to pulsate.

Both femoral arteries presented a strong but rather slow-rising pulse, and pulsation in the dorsalis pedis arteries was easily felt. A murmur was heard maximally at the base of the neck in the angle between the right sterno-mastoid muscle and the clavicle. It was loudest in systole and prolonged almost or quite into diastole, resembling to several observers the murmur of a patent ductus arteriosus. It was conducted up the neck as far as the angle of the jaw on the right, and a little way up on the left, down the right border of the sternum as far as the fourth space, and over the manubrium. A thrill, localized at the base of the neck, accompanied it, but there was no pulsation in this region. An unexplained systolic murmur was also heard below the angle of the left scapula; it is not clear that any other signs of anastomoses were sought. The Pachon oscillometer reading showed small pulsations from both arms. The maximal pulsation occurred at 60 mm. in the arm and at 100 mm. in the leg. The systolic blood pressure in the legs varied between 130–150 mm.

When the patient was previously admitted in March 1931, her signs were a little different. At that time very slight pulsation was felt in both radial and carotid arteries and the blood pressure in the arms was recorded at 70 to 80 mm. Dilatation of the aorta, as revealed to X-ray, was then not quite so great. Vision at this time was good and the fundus oculi was normal on both sides.

The urine contained neither blood nor albumin; renal function tests were not done.

Abstract of Dr. Giffin's Case

Case 3. A woman, aged 19, came to hospital in December 1938 because of headaches and failing vision.

In the spring of 1938 she began to have attacks of blurred vision lasting for one or two minutes. These episodes increased in frequency until August 1938, when she was confined to bed. Since then she had returned to limited activities and could read except during daily transitory attacks. Her sight was poorest on rising and improved during the day. She also complained of bilateral frontal headaches for several years and occipital headaches intermittently for nine months. Vomiting had occurred occasionally. The family history was not significant. She was normal at birth but was weak and under-developed in childhood. Later, owing to weakness, she was never able to do housework. Her hands and jaws fatigued easily and she had always been pale.

Condition.—The patient was mentally retarded and physically under-developed. Her central nervous system was normal. Her face and mucous membranes were pale.

Pulsation could not be felt in the left radial, brachial, subclavian, or carotid arteries. It was also absent in the right radial, brachial, and subclavian arteries, but in the right carotid artery diminished pulsation with a slight thrill was felt at the level of the cricoid cartilage, and a loud continuous bruit was heard

at this point. Photographic record of the murmur showed that it was continuous throughout the cardiac cycle, and it was thought to indicate the presence of arterio-venous fistula. Pressure medial to the right carotid artery, however, stopped the murmur without significant alteration in the heart rate. The pulsation of the abdominal aorta and its branches was somewhat increased. In the legs oscillometer excursions were normal and the blood pressures varied from 175–190 systolic and 90–110 diastolic. Skin temperatures of the fingers of both hands were consistently lower than those of the toes.

The heart was normal in size. A systolic murmur maximum in the second left interspace was heard and the pulmonary second sound was accentuated. X-ray revealed a relatively small heart, the absence of an aortic knob, and a prominent pulmonary conus. There were no cervical ribs, no rib notches, and no bony erosion in the cervical region. Radiograms of the skull were normal. The electrocardiogram revealed nothing diagnostic and the Wassermann reaction was negative.

Examination of the ocular fields showed an " upper altitudinal " scotoma on the left. Vision was 6/30 in the left eye and 6/10 in the right eye. There was no papillœdema. Fragmentary flow of blood was seen in the retinal veins and also several ischæmic areas were found. Retinal pressures, measured by an indirect method were found to be less than 20 mm. of mercury on the right and were unobtainable on the left.

Summary

A patient is described in whom the pulses of the neck and arms had been lost, and who presented signs suggesting an arterio-venous fistula at the root of the neck. The defective blood supply to the upper parts of the body was responsible directly or indirectly for a gross defect of vision, for frequent fainting attacks and headaches, and for pain in the right arm during work. The blood pressure in the patient's legs was raised.

Another case of a very similar kind is described, and a third recorded by Giffin is compared with them.

The three cases show so much in common as to suggest a pathological entity hitherto unrecognized and still awaiting dissection before its precise form can be understood.

References

Cohen, H., and Davie, T. B. (1933). *Lancet*, **1**, 352.
Giffin, H. M. (1939). *Proc. Staff Meet. Mayo Clinic*, **14**, 561.
Goldblatt, H., Kahn, J. R., and Hanzal, R. F. (1939). *J. exper. Med.*, **69**, 649.
Kampmeier, R. H., and Neumann, J. F. (1930). *Arch. intern. Med.*, **45**, 513.
Lewis, T. (1933). *Heart*, **16**, 205.
Maurer, E. (1939). *Amer. Heart J.*, **17**, 716.

THE CONDUCTING SYSTEM OF THE VERTEBRATE HEART*

BY

FRANCIS DAVIES

From the Department of Anatomy, University of Sheffield

Received April 24, 1942

A study of the comparative anatomy of the conducting system of the vertebrate heart reveals that the phylogenetic evolution of this system affords a further illustration of the dictum on the close correlation between form and function enunciated by John Hunter. My present thesis is this. A cardiac conducting system, consisting of specialized muscle (i.e. nodal tissue and Purkinje fibres), is limited to mammals and birds. The general topography of this system is closely similar in these two classes of warm-blooded vertebrates; the main differences can be correlated with different functional requirements. This system is a neomorphic development; it is not a " remnant " of more extensive tissues of similar structure in lower vertebrate hearts. The system has undergone parallel evolution in mammals and birds in response to functional requirements. The evidence in support of this thesis may be briefly summarized as follows.

MAMMALS

The sinu-atrial (S-A) node, the site of initiation of the impulse for cardiac contraction (pace-maker), was originally described by Keith and Flack as lying superficially beneath the epicardium in the upper part of the sulcus terminalis, adjacent to the end of the superior vena cava. Subsequent studies have shown that the node is a much more extensive structure, being horse-shoe shaped, and embracing the ventral aspect of the end of the superior caval vein, the anterior limb of the horse-shoe extending caudally over more than the upper half of the sulcus terminalis (Fig. 1). Moreover, the node extends through the entire thickness of the atrial wall, from epicardium to endocardium. Some investigators have claimed that, after removal of the entire node, normal cardiac rhythm is maintained; they have therefore postulated the existence of other (ectopic) centres in the atria with the same rhythmic properties as the node. Owing to the difficulty of complete removal of this extensive node, and since even a small portion of nodal tissue left behind will be capable of initiating atrial contraction, the validity of such experimental work, not subejcted to strict histological control, is open to serious question.

* Abridged form of the Hunterian Lecture delivered at the Royal College of Surgeons of England, February 9, 1942.

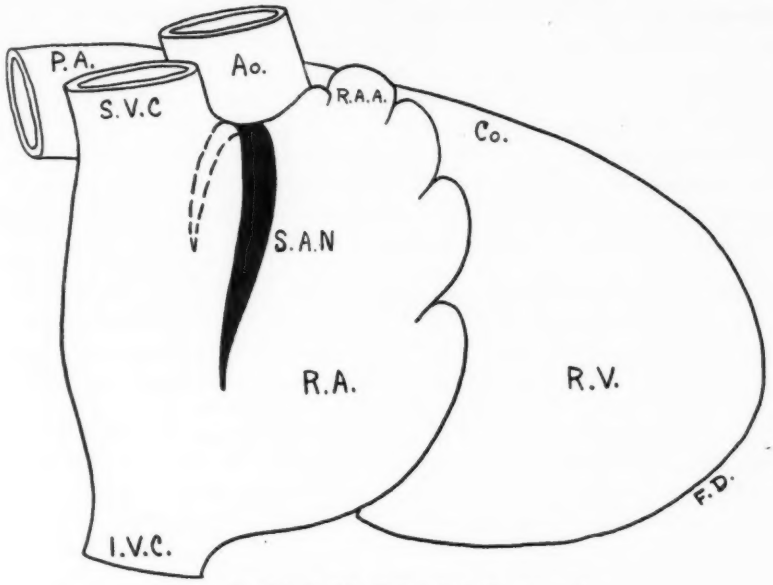


FIG. 1.—Extent of the S-A node in the mammal.

Ao., aorta; Co., conus arteriosus; I.V.C., inferior vena cava; P.A., pulmonary artery; R.A., right atrium; R.A.A., right atrial appendix; R.V., right ventricle; S.A.N., sino-atrial node; S.V.C., superior vena cava.

The node was described by its discoverers as a plexiform mass of peculiar pale-staining fibres intermingled with connective tissue and nerves; they considered this tissue to be intermediate in structure between nerve and muscle, and therefore gave it the non-committal name of "nodal tissue." Silver impregnation methods clearly reveal, however, that the nodal fibres are specialized cardiac muscle fibres; they are completely cross-striated, fusiform, and branched, their chief distinguishing character being their small breadth in comparison with the ordinary atrial muscle. This is one of the features to be correlated with the special properties of the node, namely its greater rhythmicity and slower rate of conduction than ordinary heart muscle. These nodal fibres are directly continuous with the neighbouring myocardial fibres of the right atrium; the latter are continuous with those of the left atrium; the cardiac impulse is thus transmitted through the atria by the ordinary cardiac muscle and reaches the atrio-ventricular node, whose specialized fibres are continuous with the myocardial fibres of both atria in the atrial septum.

A few observers have described a direct connection, by means of nodal tissue or Purkinje fibres, between the S-A and A-V nodes; most workers have failed to find such. Many investigators have noted the presence of typical large Purkinje fibres beneath the endocardium in both atria. From their descriptions these appear to be isolated collections of Purkinje fibres, unconnected with either the S-A or A-V node; moreover, the sites at which they have been found

vary with the observers. We ourselves have seen a small collection of Purkinje fibres beneath the epicardium in the right atrium of the ox heart, which was continuous with the caudal end of the S-A node. It is probable that these conditions should be regarded as " variations," such as would be prone to occur in a newly evolved system.

The atrio-ventricular (A-V) node, smaller than the S-A node, is situated in the lower and dorsal part of the atrial septum, with whose musculature the special nodal fibres are continuous. The node is directly continued into the A-V bundle, which runs along the upper border of the ventricular septum to the lower edge of the pars membranacea septi, and there bifurcates into right and left limbs, the bifurcation straddling the upper border of the muscular part of the septum. The right limb runs down, in the form of a round bundle, on the right side of the septum, covered over by the endocardium and a thin layer of septal myocardium, making for the septal attachment of the " moderator band." The latter in most cases conveys the right limb across the ventricular cavity to the base of the anterior papillary muscle, where the limb divides into a plexus of Purkinje fibres which ramify beneath the endocardium throughout most of the right ventricle. Very rarely, the right limb passes from the septum to the opposite wall of the ventricle independently of the " moderator band," a feature that may be attributable to variation. The left limb, in the form of a broad flattened band, descends beneath the endocardium on the left side of the septum and, at a varying distance down the septum, divides into two or more branches, each of which, after a short course down the septum beneath the endocardium, subdivides into a number of branches. These latter are conveyed by the trabeculæ carneæ and the " false tendons " across the cavity to the papillary muscles on the opposite wall, there dividing into a plexus of Purkinje fibres which ramify beneath the endocardium throughout most of the left ventricle.

The A-V node, the A-V bundle and its limbs, together with the subendocardial Purkinje plexuses are surrounded by a fibrous sheath, which both mechanically protects the relatively (but not absolutely) stationary specialized elements from friction against the vigorously contracting ventricular myocardium, and also *insulates* them from the neighbouring cardiac muscle. Into the potential space between the sheath and the specialized muscle, fluids like indian ink can be injected, and the whole ventricular ramifications of this system can thus be readily and rapidly displayed. This method cannot be successfully employed in the human, because the sheath is extremely thin and ruptures with very slight increase in pressure, allowing the injection fluid to diffuse beneath the endocardium. Until recently, the subendocardial Purkinje fibres were thought to become continuous with the ventricular muscle immediately adjacent, which latter would thus convey the cardiac impulse through the thickness of the ventricular walls: but they themselves have now been shown (in a number of mammals) to penetrate throughout the entire thickness of the ventricular walls, including the septum, surrounded by their fibrous sheath, and to become continuous with the ordinary muscle at various depths from the surface; many of them penetrate the walls in relation to the branches of the coronary arteries.

It may be observed that this discovery was made subsequent to the demonstration of a similar, but more widespread, penetration of Purkinje fibres in both ventricles and atria in the bird's heart. In the human, the ventricular Purkinje fibres are limited to the subendocardial plane. The Purkinje fibres that penetrate into the ventricular septum from the subendocardial plexuses on either side, communicate in the substance of the septum. Thus after damage of the upper part of the right limb of the A-V bundle for instance, the impulse can pass down the intact left limb, through these communicating septal Purkinje fibres to the right ventricle, reaching the latter after a delay that is very slightly greater than normal.

The discoverers of the S-A node remarked on its close similarity in histological structure to that of the A-V node, and it appears to have been generally accepted that the two nodes are identical in structure. The specialized muscle fibres of the A-V node, however, while completely cross-striated and more slender than the ordinary heart muscle, differ from those of the S-A node in being more cylindrical, more branched, and broader. These are some of the differences, to which may be attributed a probable lower rhythmicity than the S-A node and the fact that the cardiac impulse normally originates in the S-A rather than the A-V node.

In most mammals the A-V bundle and its two limbs consist of typical large Purkinje fibres. In the human, however, the fibres of the A-V bundle and of the proximal parts of its two limbs closely resemble the ordinary ventricular muscle fibres, as revealed by ordinary laboratory stains; in fact, the bundle fibres are slightly narrower than the myocardial fibres, and it is not until some distance down the septum that the typical large Purkinje fibres make their first appearance in the limbs. The pathologist may have difficulty in identifying these structures in isolated sections of the human heart; tracing continuity in serial sections is the only certain means of identifying them. The nodes, bundle, limbs, and terminal Purkinje fibres are accompanied by nerves, and numerous nerve cells are closely related to the nodes and bundle; these neural elements are capable of altering the degree of activity of the specialized conducting muscle under varying conditions. Although Kent described "accessory muscular connections" between the atria and ventricles in some mammals (rat and young rabbit; to a lesser extent, guinea-pig and hedgehog; very few in monkeys), the general opinion is that the A-V bundle constitutes the sole muscular A-V connection in higher mammals.

Birds

The bird's heart resembles that of the mammal in being four-chambered, with complete atrial and ventricular septa. The heart rate, however, is considerably faster than that of a mammal of approximately the same size, and the necessity arises therefore for a more rapid spread of the cardiac impulse throughout the entire avian heart. Although Keith, Mackenzie, and others denied the existence of specialized nodes and bundle in the bird's heart, it has been shown (Davies) that not only are such structures present, but that the specialized conducting muscle is more widely distributed in the avian than in

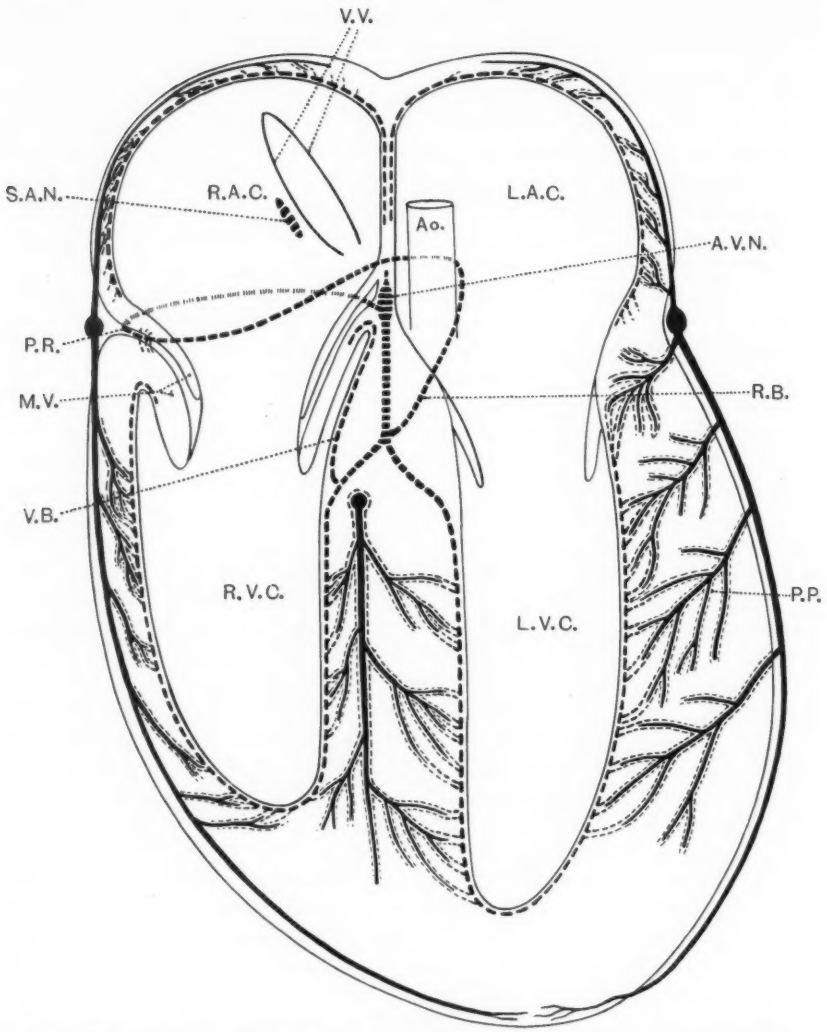


FIG. 2.—Diagram summarizing the main topographical disposition of the avian conducting system. For abbreviations see Fig. 3.*

the mammalian heart, and this latter is to be correlated with the need for more rapid diffusion of the impulse, as indicated above.

The S-A node, similar in structure to that of the mammal, lies on the right side of the entry of the right anterior vena cava into the right atrium, and extends throughout the entire thickness of the atrial wall. Unlike the mammal, however,

* I am indebted to the Editors of the *Journal of Anatomy* and to the Council of the Royal Society for permission to reproduce Fig. 2 and 3 respectively.

the nodal fibres are continuous with large Purkinje fibres, which ramify beneath the endocardium throughout most parts of the right and left atria, and penetrate the atrial walls to become continuous with the ordinary atrial muscle, but are absent from the lower part of the atrial septum, so that, as in the mammal, the specialized fibres of the A-V node establish continuity with the ordinary cardiac muscle of the atrial septum.

The A-V node is similar in structure and position to that of the mammal and is continued directly into the A-V bundle. The latter, unlike the mammalian bundle, runs caudally and ventrally into the depth of the ventricular septum, lying approximately midway between its right and left surfaces. About one quarter of the way down the septum, the bundle divides into right and left limbs; these approach the corresponding sides of the septum and there divide into a plexus of Purkinje fibres, which ramify beneath the endocardium throughout most of the ventricular chambers, also penetrating through the thickness of the ventricular walls, mostly in relation to the coronary vessels, and becoming continuous with the ordinary ventricular muscle at varying depths from the surface. In the septum, as in the mammal, communications are established between the Purkinje fibres derived from the subendocardial plexuses on either side.

The difference in position of the mammalian and avian bundle in relation to the ventricular septum can be explained by the difference in the morphology of the septum in these two classes of warm-blooded vertebrates. The A-V bundle and its two limbs in the avian heart consist of large typical Purkinje fibres. A striking example of the effect that functional requirement exerts on the topographical distribution of the conducting elements is seen in relation to the right A-V valve in the bird. In the mammal the tricuspid valve is a fibrous structure and closes passively by the pressure of the blood on its under surface during ventricular systole. In the bird this valve is a strong muscular structure, consisting mainly of an inflection of the base of the ventricle, covered on its inner surface by a thin prolongation of the atrial muscle, the epicardial connective tissue in the coronary sulcus being invaginated between the two. It is necessary that this muscular valve should contract actively at the outset of ventricular systole, and to this end early outgoing branches of the conducting system to the valve are present in the form of the right A-V ring of Purkinje fibres from the A-V node, which runs partly round the A-V orifice in the connective tissue of the valve, and an early branch from the right limb of the A-V bundle (see Fig. 2).

In the main then, the specialized conducting systems of mammalian and avian hearts are closely similar; differences can be correlated with different functional requirements.

Lower Vertebrates and the Phylogeny of the Conducting Systems of Mammalian and Avian Hearts

A number of workers, in particular Keith and Mackenzie, maintain that the nodes and A-V bundle of the mammal are remnants of more extensive tissues of similar structure in lower vertebrates. Thus, in the heart of the fish they

describe a ring of nodal tissue at the junction of sinus venosus and atrium, in the base of the venous valves, and a similar ring at the junction of atrium and ventricle. To these nodal rings are attributed a greater rhythmicity and a slower rate of conduction of the cardiac impulse than the ordinary cardiac muscle; the latter property being responsible for the delay in the passage of the impulse from one cardiac chamber to the next: this delay is necessary in order that the chamber receiving blood may become completely filled before it in turn begins to contract. Keith and Mackenzie maintain that as one ascends the scale of animals the concentration and reduction of this tissue becomes more marked. Such concentration is already present in amphibia and becomes more marked in reptiles, in which the S-A ring is reduced to a collection of nodal tissue on the left side of the sinu-atrial junction. In mammals, associated with the development of fibrous rings separating the atrial from the ventricular musculature, the A-V ring of nodal tissue is reduced to the A-V node and A-V bundle, while the S-A nodal ring is concentrated to the S-A node.

Recent detailed examination of the heart of the spotted salamander (Davies and Francis) has thrown doubt upon this interpretation of the phylogenetic origin of the specialized conducting tissue of the mammalian (and avian) heart. This animal, a caudate amphibian, has a very primitive form of heart (Fig. 3), suitable for comparison with those of fish on the one hand and those of reptiles, birds, and mammals on the other. In it the four primary chambers (sinus, atria, ventricle, and bulbus) are well defined separate structures. No specialized muscle (i.e. nodal tissue or Purkinje fibres) is present in any part of this heart, either in the walls of the chambers or at the sites of junction of the several chambers. The cardiac muscle has the same histological structure throughout, as revealed by staining with hæmalum and eosin, Van Gieson and iron hæmatoxylin, and with Bodian activated protargol techniques. The arrangement of the muscle fibres, however, is noteworthy. With the exception of the bulbus, in which the cardiac muscle is circular throughout, the musculature of the chambers is arranged in a basket-work fashion.

At the sinu-atrial, atrio-ventricular, and ventriculo-bulbar junctions, however, the muscle fibres become abruptly changed to a circular arrangement, the sudden change in direction being a striking feature at each of the junctional sites. In each of these rings (of ordinary cardiac muscle) the fibres branch, the branches connect with the adjacent fibres, and this has the effect of converting these morphological rings into physiological spirals. The time taken by the cardiac impulse to traverse these spirals will, we believe, account for the delay in the passage of the impulse from one chamber to the next, without postulating the existence of special nodal (or block) fibres at these junctional sites. The analysis of superimposed tracings of the outlines of the heart of the salamander, made from slow-motion cinephotographic records of the normally beating heart, enables the course of the wave of contraction and the phases of a complete cardiac cycle to be determined. Such records indicate that the phases of the cardiac cycle in the heart of the salamander are similar to those of the mammalian heart. While similar detailed study of the hearts of fish (eel, gurnard), amphibia (frog) and reptiles (tortoise, Mississippi alligator, Sphenodon) still

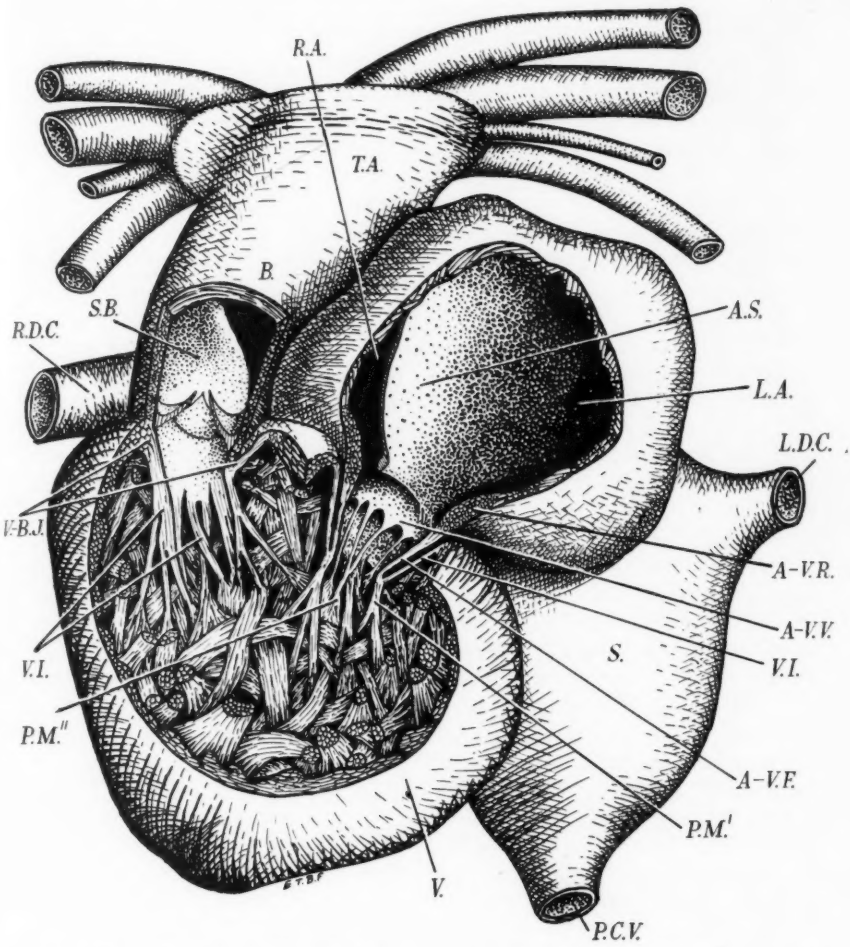


FIG. 3.—Dissection of the salamander's heart, showing atrio-ventricular and ventriculo-bulbar junctions.

A., atria; Ao., aorta; A.S., atrial septum; A-V.F., atrio-ventricular funnel; A-V.J., atrio-ventricular junction; A-V.N., atrio-ventricular node; A-V.R., atrio-ventricular ring; A-V.V., atrio-ventricular valve; B., bulbus; Co., conus arteriosus; I.V.C., inferior vena cava; L.A., left atrium; L.A.C., left atrial cavity; L.D.C., left duct of Cuvier; L.V.C., left ventricular cavity; M.V., muscular valve; P.A., pulmonary artery; P.C.V., post-caval vein; P.M.′ and P.M.″, papillary muscles; P.P.F., penetrating Purkinje fibres; P.R., right A-V Purkinje ring; R.A., right atrium; R.A.A., right atrial appendix; R.A.C., right atrial cavity; R.B., recurrent branch of A-V bundle; R.D.C., right duct of Cuvier; R.V., right ventricle; R.V.C., right ventricular cavity; S, sinus; S-A.J., sinu-atrial junction; S-A.N., sinu-atrial node; S.B., septum bulbi; S.V.C., superior vena cava; T.A., truncus arteriosus; V., ventricle; V.B., branch of right limb of A-V bundle to muscular valve; V-B.J., ventriculo-bulbar junction; V.T., ventricular trabeculæ; V.V., venous valves. (Abbreviations for Fig. 2, 3 and 4).

await completion, preliminary inspection of sections of these has failed to reveal the presence of nodal tissue or Purkinje fibres in any part of these hearts.

The conclusion is thus reached that the nodes and A-V bundle (together with its two limbs and the terminal subendocardial and penetrating Purkinje fibres) in the hearts of mammals and birds are neomorphic developments, which have undergone parallel evolution in association with the more rapid rate of the heart in proportion to its size, in these homoiothermal vertebrates. The heart rates of the frog, mouse, and canary are roughly 30 (at 15° C.), 700, and 1000 beats a minute respectively. These hearts are approximately of the same size and the cardiac impulse has therefore to be propagated throughout the heart more rapidly in the mouse than the frog, and more rapidly still in the canary. It might be expected that, whereas the ordinary cardiac muscle may be capable of conducting the impulse rapidly enough in the frog, special tissue which can conduct the impulse much more rapidly might be developed in the mouse and canary, and that this tissue would probably have a more extensive distribution in the bird than in the mammal. Such has been shown above to be the case.

When the sinus, atria, ventricle, and bulbus of the frog's heart are separated from each other by cuts made accurately through the junctions of these chambers, it is found that rate of rhythmic contraction of these chambers diminishes progressively from sinus to bulbus. In the absence of histologically specialized muscle, no satisfactory explanation of this difference in the intrinsic rhythmic rates of the several cardiac chambers has been advanced. Recent estimations of the relative glycogen content of the muscle fibres of these chambers have been made by staining sections with carmine, tracing the outline of the (highly magnified) fibres on squared paper and plotting in the red-stained glycogen. The glycogen is found to increase progressively from sinus to bulbus (Davies and Francis, 1941) (Fig. 4). This order of increase is the same as that of the density and compactness of the cardiac musculature and of the work done by the several chambers, so that a positive correlation in this respect may be made, the glycogen possibly being a source of energy for the work of contraction. But the intrinsic rhythmicity diminishes in this order; whether this relation is merely coincidence or indicates a causal relationship remains to be determined. In the mammal, the nodes are particularly poor and the Purkinje fibres rich in glycogen in comparison with the ordinary cardiac muscle. The glycogen content of the muscle fibres at the S-A and A-V junctions of the frog's heart is intermediate between that of the muscle fibres of the adjacent chambers, and this may be taken as collateral supporting evidence that this junctional muscle is not the same as the nodal tissue or Purkinje fibres of the mammal.

Further collateral evidence that the nodes and bundle of the mammal are newly evolved structures is afforded by a study of their ontogeny in the calf heart. Shaner found that, in the 9 mm. calf embryo, the A-V node appears behind the dorsal endocardial cushion and from it the A-V bundle grows on the top of the ventricular septum. At this time the developing musculatures of the atria and ventricles are continuous round the coronary sulcus. The A-V node and bundle thus appear and grow like any other embryonic organ

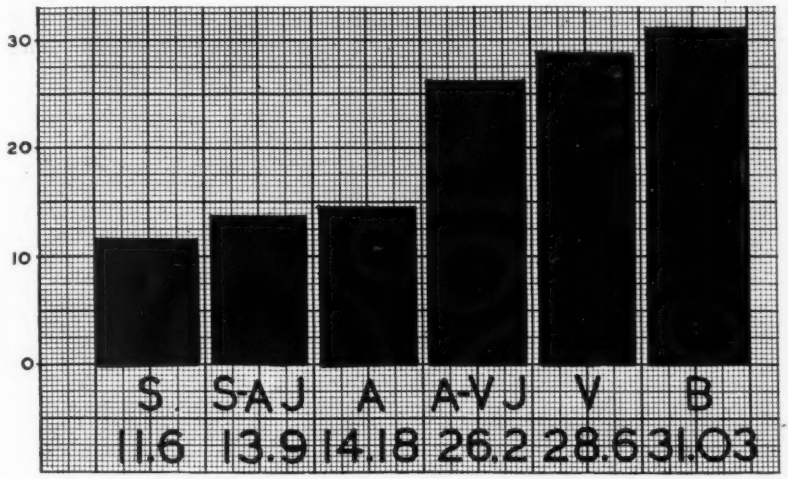


FIG. 4.—Glycogen content of the frog's heart. The relative amounts of glycogen in the muscle fibres of the cardiac chambers has been estimated graphically from sections stained by Best's alkaline carmine.

and are not remnants of more extensive tissues connecting the atria and ventricles at an earlier stage of embryonic life. Similar remarks apply to the appearance of the S-A node at a later date (100 mm.).

SUMMARY AND CONCLUSIONS

1. The specialized muscle fibres comprising the conducting system of the hearts of mammals and birds include S-A node, A-V node, A-V bundle and its two limbs, and terminal ventricular subendocardial and penetrating Purkinje fibres. Added to these in the bird's heart are the atrial subendocardial and penetrating Purkinje fibres, the right A-V ring, and the special branch of the right limb of the A-V bundle to the muscular A-V valve.

While the main topography of this system is similar in mammals and birds, differences are correlated with functional requirements.

2. The specialized cardiac conducting system of these homoiothermal vertebrates is not a remnant of more extensive tissues of similar structure in lower vertebrate hearts. It is a neomorphic development, associated with the more rapid rate of the heart (more rapid, in proportion to its size). Ontogenetic development of these structures in the mammal (calf) supports this view.

3. In a lowly generalized vertebrate heart (Salamander) no specialized tissue is present. The sequences of the cardiac cycle are similar to those of the higher vertebrates. Each chamber has its own intrinsic rhythmic rate, the reason for which is not clearly established. The glycogen content of the musculature of the heart of the frog, which is also devoid of specialized tissue, is inversely proportional to the intrinsic rhythmic rates of the several chambers.

4. In mammals and birds, parallel evolution of the specialized conducting system has taken place; small differences in the topography of the specialized conducting fibres in closely allied species, or in different animals of the same species, may be attributed to variation.

References

In this brief survey no attempt is made to incorporate all revelant bibliographic references, which will be found in the works cited below.

Blair, D. M., and Davies, F. (1935). *J. Anat., Lond.*, **69**, 303.
Davies, F. (1930). *Ibid.*, **64**, 129 and 319; and (1931), **65**, 339.
—— and E. T. B. Francis (1941). *Phil. Trans. Roy. Soc.*, B., No. 578, **231**, 99.
—— —— (1941). *J. Physiol.*, **100**, 329.

THE SINO-AURICULAR NODE:
A HISTORICAL NOTE

CONTRIBUTED BY

ARTHUR KEITH

The Editors of the *British Heart Journal* have reason to pride themselves on the publication of this article in which Professor Francis Davies sums up the results of a long and careful examination of the conducting muscular system of the vertebrate heart. He has made discoveries of outstanding importance —especially the existence in the bird's heart of a system more highly evolved than even that of the mammalian heart (which Dr. Ivy McKenzie and I had searched for and missed); no less outstanding in importance is his success in following the ultimate branches of the A-V bundle to their termination in the ventricular musculature.

While reading the proof sheets of Professor Davies's article, there came back to me the memory of a letter I received from the late Sir James MacKenzie (then in Burnley) informing me of Tawara's discovery of the A-V conducting bundle in the mammalian heart. The letter came late in 1905 or early in 1906. I had then been at work on the anatomy of the heart for five or six years,* and thought I knew all that was to be found in that organ. Indeed, I was so sceptical of the existence of the bundle that I had drafted a letter to the *Lancet* denying its existence but, fortunately for me, made one more search before committing myself, and found in the human heart all as Tawara had described it, and then wondered how I had missed a structure that was so evident—when once seen. So the letter was amended and dispatched (*Lancet*, 1906, 1, 623). I took the lesson as a warning and yet repeated the mistake a few years later when searching for an A-V system in the bird's heart. Probably my microscopic technique was at fault; I have always envied men who were masters of microscopic technique—almost as much as I envied my friends who could hold free converse in foreign languages.

My partnership with MacKenzie of Burnley must have begun about 1904; he sent me hearts of his more famous cases to see if I could find a pathological basis for their irregularities. I dissected and drew them, cut sections of all parts, but after many months of close observation got no definite correlation between the type of arrhythmia and a pathological lesion, so great was the variation in microscopic appearance as I went from heart to heart. But one thing I did find that afterwards proved to be of significance. At the time

* Readers will find my work of that time buried in the *Proceedings of the Anatomical Society* (published in the *Journal of Anatomy*), from 1902 onwards.

we were all impressed by the fact that in lower vertebrates the contraction wave of the heart was initiated in the *sinus venosus*. Hence in cutting MacKenzie's hearts I made my sections so as to expose the remnants of the sinus which are included in the right auricle. In all my sections which traversed the sulcus terminalis where the superior vena cava entered the right auricle (the sulcus marking the infolding of the sinus) I noted a localized density of tissue in which nerve fibres seem to terminate. So variable was this structure in its density and form in hearts that had manifested irregularities of rhythm and in others that were reputed to have been normal in action, that I passed it by as having no functional significance. This was before Tawara had made his discovery.

At that time my wife and I rented a farmhouse in Kent, where we spent vacations. We lived near the village of Bredgar, famous for its cherry orchards; a neighbouring village was Borden where lived the Flack family. We heard that Martin Flack, just down from Oxford, was looking for a hospital at which to continue his medical studies and lost no time in putting before him the attractions of the London Hospital, where I taught anatomy and Leonard Hill physiology. Martin joined us; indeed he became more Hill's pupil than mine. His was a most attractive personality, fair haired, clean skinned, bright-eyed, short and sturdy—my ideal of a Saxon youth; merry, ever ready for work or play; as true and lovable a man as I have met.*

In the long vacation of 1906, Flack and I turned my study at Bredgar into a laboratory—microtome, oven, microscopes; we had a vast store of human hearts and were trapping moles, rats, mice, and hedgehogs with the intention of verifying and extending Tawara's discoveries on their hearts. I remember well one very hot day, late in the summer of 1906, my wife and I going out on our bicycles leaving Martin running serial sections of a mole's heart. On returning he bade me look through a microscope at a strange structure he had found at the junction of the superior cava with the right auricle. The structure was muscular but quite different from the musculature round about. I remembered the body I had seen in the MacKenzie hearts; we set to work and found it at the same site in all the mammalian hearts at our disposal. In structure it resembled the node of Tawara; hence we *inferred* it to be the site at which the cardiac rhythm was normally initiated (*J. Anat.* (1907) 41, 173).

That is the beginning of our knowledge of the S-A node in the rough. Professor Davies has produced the finished article. Yet there are one or two points in his account that leave me unsatisfied. There is the relation of nodes to nerves which is left untouched. There is the secretory side of nodal function to be considered—or rather the excretory or secretory hormone formed at neuro-nodal junctions. Therein lies the central nervous control of the cardiac rhythm. After all, nerve cell and muscular cell have a common ancestry and there is still room to believe there may be cells which retain the common ancestral qualities of irritability and contractibility and that nodal cells do retain these original characters. I wish someone would again examine the sino-auricular

* In the 1914-18 war, Dr. Flack became scientific advisor to the Medical Department of the embryonic R.A.F. He died August 16, 1931, just when his great ability was meeting with a wide and deserved recognition.

node of Ornithorychus; my sections are lost, but I believed I could trace in them a direct continuity of nerve fibre and nodal cellular element.

Professor Davies regards the muscular connecting system of the mammalian and avian heart as a new formation—one which appeared in the evolution of animals at the same time as a temperature regulating system. Such a sudden appearance would be an example of emergent evolution—a form of evolution I have the same antipathy to as I have for miraculous happenings of all kinds. They are made believable by blanks in our knowledge. We know enough to reject the idea that warm-blooded beasts appeared suddenly; there are still intermediates in this respect—the Monotremes. I agree that heart action and body temperature must have been coordinated in their evolution, but, although the detection of the coordinating mechanism in the evolving or developing animal body still eludes us, that in no wise shakes our confidence that it exists and will be discovered. And its foundation will be found not in something interpolated but in an emergence from something that has gone before. The A-V bundle may have developed as Professor Shaner has described and still be a modification of the auriculo-ventricular function of the cold-blooded heart.

CHEST LEADS IN CONGENITAL AND ACQUIRED DEXTROCARDIA

BY

J. S. RICHARDSON

Received February 20, 1942

Four cases with hearts situated in the right side of the thorax have been seen recently in a military hospital. Two of these had true dextrocardia (Cases 1 and 2), and were admitted for diseases that did not affect the heart. One was suffering from an apical lobar pneumonia and the other from a gastric ulcer, and in each the dextrocardia was an incidental finding. There was transposition of the viscera in both, and the heart was a mirror image of the normal, as shown by screening and by X-ray films in the antero-posterior and oblique positions.

The third (Case 3) had a traction dextrocardia with cardiac dullness to the right of the mid-line. X-ray examination showed that the heart was pulled over, with the apex under the right border of the sternum, and the chambers were in their normal relationship.

The fourth (Case 4) was one of eventration of the left lobe of the diaphragm of such degree that the heart was displaced to the right of the mid-line. It was not rotated from its normal relationship to the chest wall as shown by radiography and screening, and had a perfectly normal outline.

Electrocardiograms were taken and the standard leads I, II, and III were used with the chest leads C_2F and C_4F, as laid down by the American Heart Association and the Cardiac Society of Great Britain and Ireland (1938). Two further chest leads were taken to reproduce, for the cases of true dextrocardia, the same arrangements of leads as is used with C_2F and C_4F in the normal subject: an upward deflection indicated a positive electrical potential in the heart. The lead that was equivalent to C_2F was taken from the right sternal margin in the fourth interspace, with the indifferent electrode on the right ankle, C_2F (right): the lead equivalent to C_4F was taken from the right mid-clavicular line in the fifth right interspace with the indifferent electrode on the right ankle, C_4F (right).

In Cases 1 and 2, the three standard leads were similar to those usually found in dextrocardia: all the waves in lead I were inverted and the maximum deflections were found in lead III instead of in lead II. The chest leads, C_2F and C_4F, showed inverted P and T waves. The direction of the deflection of the P wave is so inconstant in chest leads if the indifferent electrode is not

on the right arm (Deeds and Barnes, 1940), that it must be neglected in the present instance. The inverted T wave, on the other hand, is a significant feature. When the leads C_2F (right) and C_4F (right), equivalent to the chest leads C_2F and C_4F in those with normally placed hearts, were taken, the tracing was normal in all respects, and the T waves were positive or diphasic (Case 1, C_2F (right); see Fig. 1). These findings resemble those of Kossman (1940) who

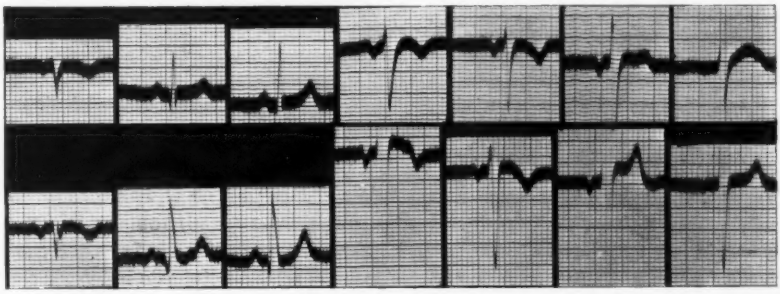


FIG. 1.—Standard and chest leads in two cases of congenital dextrocardia: Case 1 (above) and Case 2 (below). The leads are indicated below.

writes of five cases of true dextrocardia that " the T wave was isoelectric or negative in leads from the left side or middle of the chest and positive in leads from the right side."

The case with a traction dextrocardia (Case 3) had normal leads I, II, III, C_2F, and C_4F, but C_2F (right) and C_4F (right) had upright T waves. Case 4 had normal leads I, II, III, C_2F, and C_4F, and a negative T wave in C_4F (right), but a positive T was present in C_2F (right) (see Fig. 2).

It was decided to find out if normally placed hearts would give a downward deflection of T in leads C_2F (right) and C_4F (right). Cases were therefore

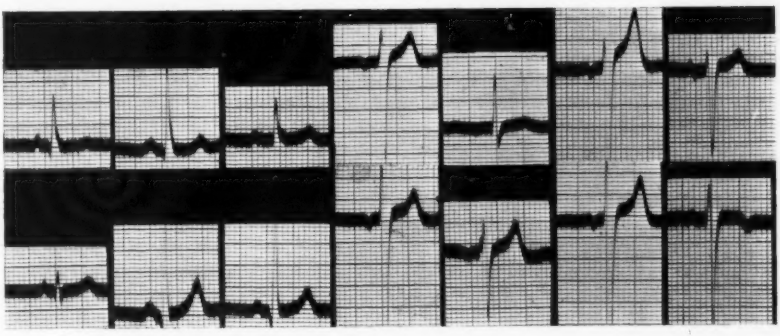


FIG. 2.—Standard and chest leads in two cases of acquired dextrocardia: Case 3 (above) and Case 4 (below). The leads are indicated below.

selected who gave no past history of rheumatism or of any other condition that might have damaged the heart, had no symptoms found in cardiac disease, had a good exercise tolerance, and hearts that were normal, clinically and radiologically. Eighteen cases were examined and gave normal tracings in the standard leads. The results in regard to the direction of the T waves were as follows:

	Positive	*Negative*	*Varying* *
C_4F	18	0	0
C_2F	15	1	2
C_2F (right)	1	14	3
C_4F (right)	0	18	0

* In these cases the T wave varied from tracing to tracing between positive diphasic and negative deflections.

Thus in the normal, C_4F always had a positive, and C_4F (right) a negative T wave, while the sternal leads were predominantly positive when taken on the left, and negative on the right. Deeds and Barnes (1940) found positive T waves in leads C_2F and C_4F in 99 and 100 tracings respectively from their 100 normal cases. They also found that T was negative or diphasic in 79 per cent of cases in lead C_1F, that is, with the chest electrode to the right of the sternum.

The two cases of dextrocardia had reversed deflections of the T wave in the chest leads as compared with the normal.

The case of traction dextrocardia showed a mixture: the direction of the T wave in leads C_2F and C_4F was positive, i.e. normal, but in the leads from the right side of the chest wall and the right ankle the direction of the T waves was also positive, thus resembling true dextrocardia.

Case 4 with a positive T in lead C_2F (right) but normal deflections in the other leads cannot be regarded as having an abnormal tracing, since the T wave in C_2F (right) was positive in one and variable in three of our eighteen normal cases and was positive in 21 per cent of Deeds and Barnes' cases.

Summary

1. Two cases of congenital dextrocardia with transposition of the viscera were found to have in chest leads T waves that had deflections in the opposite direction to the normal.

2. In two cases of acquired dextrocardia, one had T waves in leads, taken from the right side of the chest, that resembled those of congenital dextrocardia in direction, but the other conformed to the tracing found in about 20 per cent of subjects with normally placed hearts.

It is a pleasure to express my thanks to Professor W. T. Ritchie for his interest and advice, to Professor D. M. Dunlop, Director of the Clinical Laboratory, Edinburgh Royal Infirmary, for his kindness in permitting me to use the Electrocardiographic Department, and to Mr. R. P. Danskin for taking the tracings and for his generous help.

My thanks are also due to Lt.-Col. J. G. Ronaldson, R.A.M.C., for permission to forward this paper for publication.

References

Deeds, D., and Barnes, A. R. (1940). *Ibid.*, **20,** 261.
Kossman, C. E. (1940). *Ibid.*, **20,** 322.
Standardization of præcordial leads (1938). *Amer. Heart J.*, **15,** 107, 235.

ELECTROCARDIOGRAPHIC CHANGES DUE TO TRAUMA

BY

HUGH BARBER

From the Derbyshire Royal Infirmary

Received April 25, 1942

Many electrocardiograms have been recorded in cases of trauma of the heart. Beck (1935 and 1940) has studied the problem in the surgical wards and in animal experiments. Kissane (1937 and 1940) has published clinical and experimental records, and in Warburg's analysis of cases (1938 and 1940) there are his own tracings and those of other workers. Anderson (1940) published a case, with full clinical details and convincing electrocardiographic proof of myocardial injury. Zuckerman (1942) and Kessler (1941) record experiments.

From this hospital (Barber, 1938 and 1940) there are clinical notes of case histories suggesting heart trauma dating back to 1910; and there is evidence from accident autopsies (Barber and Osborn, 1941).

Both animal experiments and clinical records suggest that the electrocardiogram should be taken quite soon after the injury, because abnormalities may be in evidence only for a short time.

This paper gives an account of a series of electrocardiograms from patients, irrespective of their symptoms, who came to hospital as the direct result of a severe blow over the front of the chest, or some crushing injury of the thorax. Most of the examinations were made within a few hours of the accident and all within 48 hours; the patients being seen in the casualty department, the radiological department, or a surgical ward. The total number examined was thirty-three, in whom there were eight abnormal tracings of definite but varying significance, and two that were inconclusive.

The accidents were all from traffic or industry; not one of them was the result of enemy action. They were selected, as opportunity arose, on the basis of having sustained a reasonably severe blow or injury. All those showing an abnormal tracing were with one exception below 45 years in age, and they were active people free from degenerative processes. The youngest, aged 17 years, who developed heart block from a crushing injury of the thorax, is a good illustration of the fact that in the young and elastic chest the heart may be injured without fractures of bone.

There was rather a high proportion of seriously injured in the series, but that is to be expected, if one seeks material coming to hospital soon after

accident. There is ample evidence, in the reported cases, of heart trauma after accidents that had seemed to be comparatively trivial. One need only look at the cardiographic pictures to see that an early tracing is required.

No two accidents are quite alike, but comparison with the experimental work in animals will show that many of the abnormal tracings recorded therein have been met with in this series of hospital accident cases. Analysis of the symptoms is not profitable with a series so small and variable. Moreover, early symptoms of a cardiac lesion may have been masked by the associated injuries, and in some cases later ones kept in check by the necessary rest in bed. Some of the most convincing clinical histories suggesting myocardial contusion recount a blow or crushing injury; then an interval, variable in time, before symptoms of dyspnœa and angina develop; and perhaps no heart investigation until two or three weeks later. It is in this way that proof may be unobtainable. And by way of contrast, one or two cases in this series, with significant temporary changes in the T waves, may have shown little or no evidence from symptoms, because the associated chest injuries necessitated a rest in bed until the heart had recovered.

From the publications referred to, it is possible to find complete clinical pictures of traumatic heart lesions with history, symptoms, and signs; but this paper is confined to an analysis of the electrocardiograms in a series of accidents. There was no example of auricular fibrillation, nor was there a picture resembling coronary thrombosis. There was one example of partial heart block. These three abnormalities are the most likely to be associated with clinical symptoms of long duration in a case of trauma.

The abnormal tracings in this series have been one example of partial heart block, one of sinus bradycardia, one of slurring of the R waves, and five with temporary changes in the T waves. Two more with changes in lead III alone are considered doubtful. In view of the recent publication of White, Chamberlain, and Graybiel (1941) that the T wave in lead II may sometimes vary with a change in position of the patient, it is necessary to say that all the tracings were taken with the patient lying down. Brief notes of the cases follow.

Case Notes

Case 1. *Partial Heart Block* (Fig. 1). C. M., male, aged 17 years. On November 11, 1941, at 8.30 a.m., he was crushed between the radiator of a large lorry and a wall. He was doubled up with pain for a few minutes and coughed up a little blood-stained material. He soon recovered and cycled up to hospital. Examined at 10 a.m. there was no distress, the X-ray evidence was negative, except for slight dimness in the left lung (which passed off in two days): the pulse rate was 45 to 50, not quite regular, with a tendency to have three beats and a pause; the first sound was prolonged; there was also an occasional premature ventricular contraction. The cardiogram showed partial heart block (see Fig. 1). The blood pressure was 115 systolic and 55 diastolic. He was detained in hospital three weeks with no change in his condition or his tracing. The heart rate increased to 68 to 72. A month after the accident, he was short of breath if he walked more than a mile. Three months after he had no discomfort unless he ran, and he had started light work. Numerous tracings had shown no change in the long P–R interval. After five months the heart rate was

72, the blood pressure was 120 systolic and 80 diastolic, and the tracing unchanged, except that the P–R interval was more uniform in length, 0·35 of a second. He was working successfully but not capable of running without discomfort. He had not

FIG. 1.—Partial heart block after trauma.

had rheumatic fever or scarlet fever, and the Wassermann was negative. There was no evidence from his doctor to suggest that he had heart disease from natural causes, and he was a vigorous cyclist and player of games before the accident.

Case 2. *Sinus Bradycardia* (Fig. 2). B. F., male, aged 33 years. On February 2, 1942, he was driving a trolley-bus, which skidded and ran into a wall. He bruised his chest on the steering-wheel and was "winded," but cleared up the accident; and an hour later drove off with another bus. After driving for a quarter of an hour

FIG. 2.—Sinus bradycardia after trauma.

he fainted, quite unexpectedly. He soon recovered and was brought to hospital. Nothing abnormal was found, except for a slow heart rate of 44. He was admitted for two days; when the heart rate taken every hour varied between 36 and 46. He reported on the fifth day, free from symptoms, with a heart rate of 45 and a normal tracing. On the twelfth day the rate was 72 and he was quite well. Sinus bradycardia has been recorded in animal experiments.

Case 3. *Slurring of the R waves* (Fig. 3). F. C., male, aged 26 years. On January 18, 1939, he was struck on the front of the chest by a fall of limestone, which crushed him against a lorry. The left clavicle and the third, fourth, and fifth ribs were fractured and the left scapula. He was admitted to a surgical ward, rather shocked, with a pulse rate between 90 and 100, but no other signs of heart lesion except slurring of the R waves in all three leads. On February 2 there was no change, but on February 7 it was only definite in lead I. He went home after six weeks and was at work, feeling quite well, three months after the accident. Asked to report three years after the accident, he gave a history of excellent health and his cardiogram was normal in all four leads. Slurring of the R waves has been recorded in animal experiments.

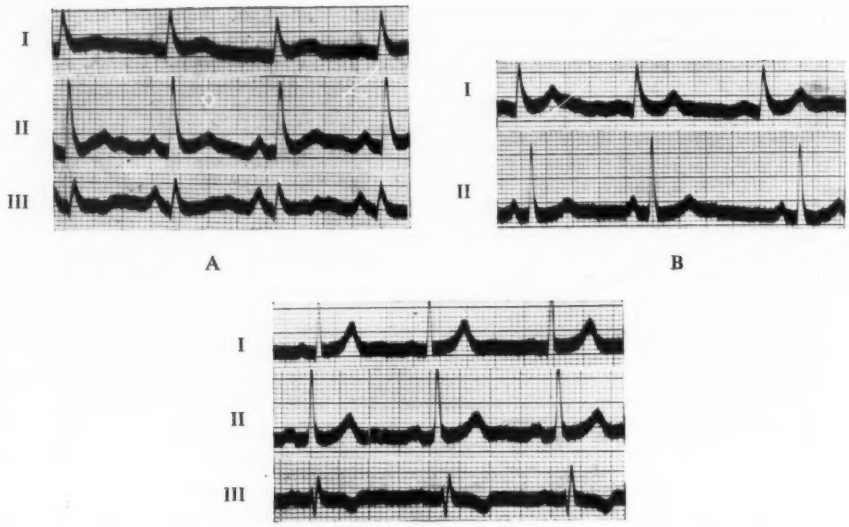


FIG. 3.—Slurring of the R waves. (A) 18/1/39. (B) 7/2/39. (C) 5/3/42.

Case 4. *T waves of exaggerated amplitude* (Fig. 4). G. W., male, aged 35 years. On January 20, 1942, he was kicked over the front of the chest by a horse, which knocked him across the stable. Seen in the Casualty Department an hour later, he

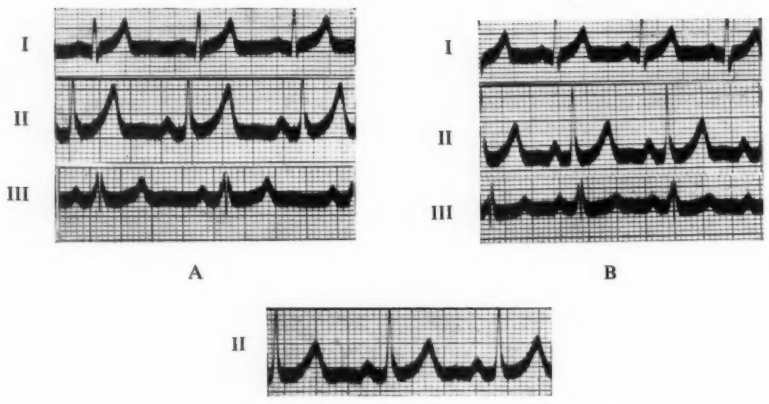


FIG. 4.—T waves of exaggerated amplitude after trauma. (A) 20/1/42. (B) 23/1/42. (C) 27/1/42.

was free from distress. The X-ray and other findings were normal, but the electrocardiogram showed T waves of an amplitude almost equal to that of the R waves. Three days later the proportions were normal; bruising was noticed around the costal

cartilages between the nipple and the sternum. Seven days after the accident the tracing was normal. There had been no symptoms of discomfort apart from the bruising. Beck (1935) has recorded this finding.

Case 5. *Temporary changes in T waves* (Fig. 5). E. D., female, aged 31 years. On December 3, 1941, she was thrown out of a motor car. There was bruising of the back and chest. Two ribs were fractured on the right side, also the right scapula and one rib on the left side. She was very distressed, with extensive lung contusion on

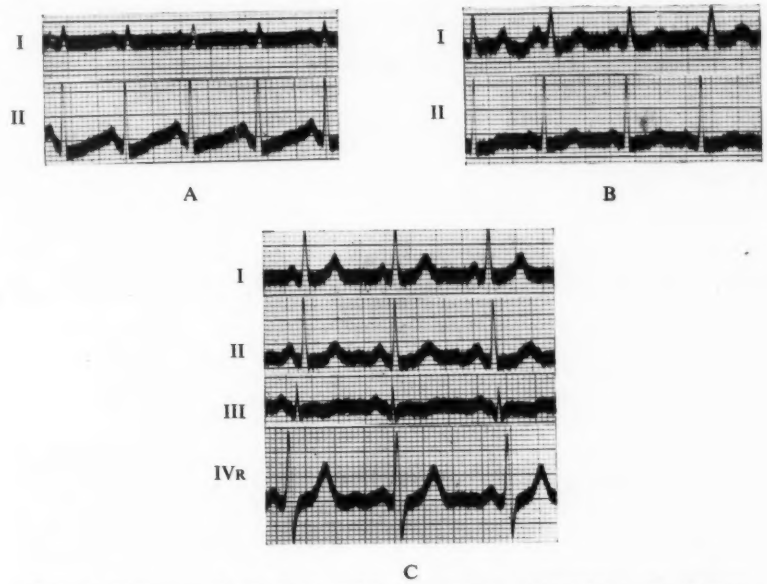


FIG. 5.—Temporary changes in T_1 and T_2 after trauma. (A) 4/12/41. (B) 15/12/41. (C) 6/1/42.

both sides and pleurisy over the left lung. The T waves in leads I and II were flat or absent. On the sixth and seventh days there was a pericardial friction sound, but this was only definite on these two days. Twelve days after the accident the T waves were upright, and after five weeks the tracing was normal in all four leads. In the fourth week, when she was well enough to screen properly, a small but definite pericardial effusion was recognizable. She travelled to her home by car thirty miles in the eighth week; and reported four months after the accident that she was getting about quite well but sometimes had a tightness in the chest if she hurried. The early return to normal of the T waves is an important observation, in view of the X-ray evidence later.

Case 6. *Temporary Changes in the T waves* (Fig. 6). J. M., male, aged 28 years. On December 4, 1941, he was felling a tree, when the trunk swung round and crushed him against the stump. He was admitted with five ribs fractured on the right side and his left scapula; also fracture of the seventh dorsal vertebra. He was admitted rather shocked with a quick heart rate. Next day the electrocardiogram showed a flat T wave in lead II, which was little improved four days later, but was quite normal on the seventeenth day after the accident. He was up in a spinal jacket in two months, and was quite well in himself three months after the accident, having exercises for the spine.

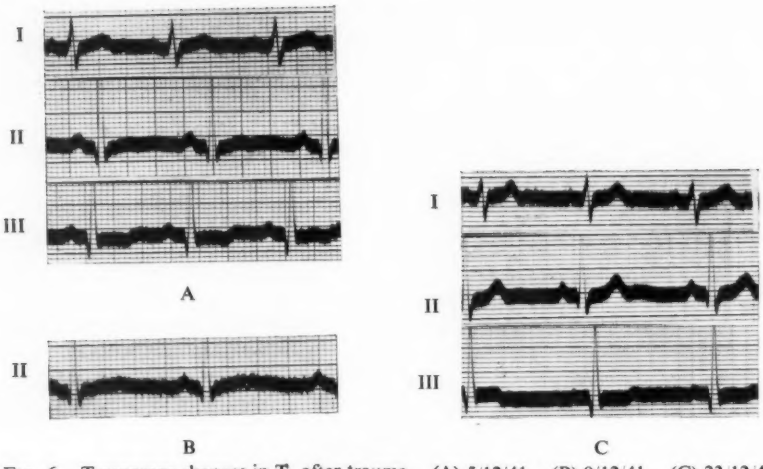


FIG. 6.—Temporary changes in T_2 after trauma. (A) 5/12/41. (B) 9/12/41. (C) 23/12/41.

Case 7. *Temporary Changes in the T waves* (Fig. 7). W. H., male, aged 62 years. On November 19, 1940, he was crushed by a fall of roof in a coal mine. He was admitted with extensive superficial bruising and some pain in the chest, but no dyspnœa. The electrocardiogram showed a flat or slightly inverted T wave in lead I. Three

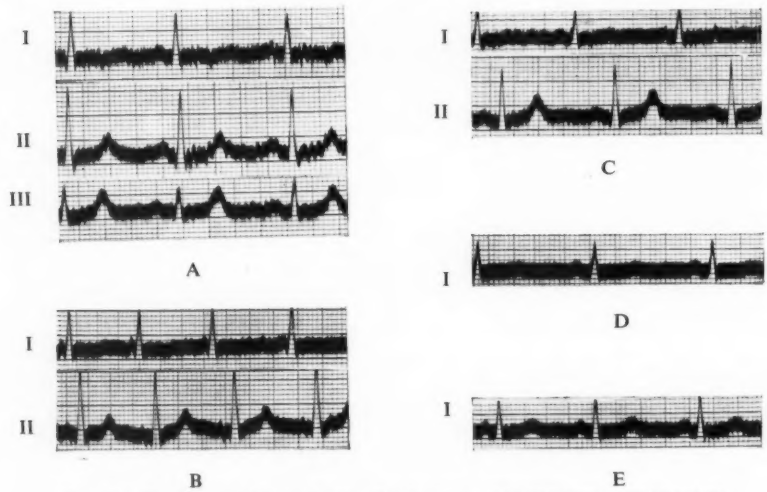


FIG. 7.—Temporary changes in T_1 after trauma. (A) 19/11/40. (B) 22/11/40. (C) 10/12/40. (D) 31/12/40. (E) 14/1/41.

days later this was unchanged. He had a large heart with the diastolic blood pressure 110 and the systolic 180. His arteries were thick and tortuous. He went home after two weeks, and subsequent tracings (Fig. 7) show the T wave improving until it was definitely upright eight weeks after the accident. In six months he was back at work again.

Case 8. *Temporary Changes in the T waves* (Fig. 8). F. M., male, aged 45 years. On March 3, 1942, he was crushed between two buffers. There was extensive bruising over the trunk, with subcutaneous emphysema over the left side. He was very shocked, with a heart rate of 100 and sometimes 140. The second, third, and fourth ribs were

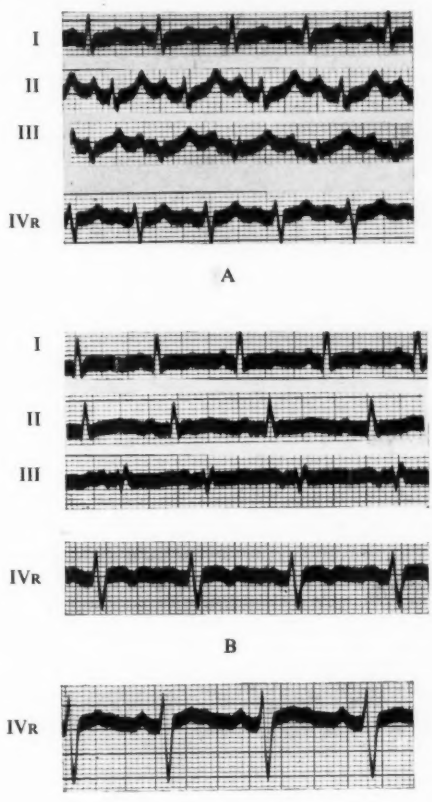


FIG. 8.—Temporary changes in T waves of all leads after trauma. (A) 10/3/42. (B) 13/3/42. (C) 16/3/42.

fractured on the left side and also the left scapula. The cardiogram a few hours after the accident was normal. Three days later his general condition was rather improved, but the tracing showed inversion of the T wave in lead IVR and the other T waves were flat (Fig. 8). In another three days the T waves were normal again. He progressed favourably and was getting about the ward by the end of five weeks.

Cases 9 *and* 10. *Temporary Changes in T wave of lead III only*. There were two examples of this, one in a man who had a large bruise over the sternum from a blow from a machine belt, and the other in a man who was crushed between two buffers. In neither case was there a fracture. Both were free from any serious symptoms.

As an explanation of this finding the possibility of a change in the height of the diaphragm must be considered. In one of them examinations could be made that appeared to exclude this, but the other was confined to bed.

Analysis of the Accidents

The accidents may be grouped rather loosely as follows:

1. Crushed by a fall of roof in a coal mine: four cases, illustrated by Fig. 7.
2. Crushed between two buffers, or similar accident: seven cases, illustrated by Fig. 1, 6, and 8.
3. Chest injuries against steering-wheel of car: one case, illustrated by Fig. 2.
4. A severe fall on to the chest: six cases, illustrated by Fig. 5.
5. Kicked on the chest by a horse: two cases, illustrated by Fig. 4.
6. A severe blow over the chest or left side: thirteen cases, illustrated by Fig. 3; in this group were the two doubtful tracings, 9 and 10, not illustrated.

It is of interest that there should be only one " steering-wheel " accident, because it is a fairly common one, of which there have been two more examples at this hospital recently. They are excluded from this series, because they did not come to hospital until the fourth week after the accident. Both had a crack in the sternum and were complaining of anginal symptoms, but the electrocardiogram was normal at this stage. One, aged 40 years, recovered completely after about six weeks, but the other, aged 51 years, complains of some limitations to his response to exertion six months after the accident. He has no claim to compensation.

Summary

A series of 33 hospital accident cases has been examined within two days of the injury. Patients with a severe blow over the chest or a crushing injury of the thorax were selected as opportunity arose.

Eight abnormal electrocardiograms were obtained. The changes observed are comparable with results obtained in animal experiments.

My thanks are due to my surgical colleagues and to Mr. G. Lovell Stiles for his help in the X-ray department and with the tracings.

References

Anderson, R. G. (1940). *Brit. med. J.*, **2**, 307.
Barber, H. (1938). *Ibid.*, **1**, 433.
—— (1940). *Ibid.*, **2**, 520.
—— and Osborn, G. R. (1941). *Brit. Heart J.*, **3**, 127.
Beck, C. S. (1935). *J. Amer. med. Ass.*, **104**, 109.
—— (1940). *Diagnosis and Treatment of Cardiovascular Disease.* Edited by Stroud, Philadelphia, vol. 2, p. 1157.
Bright, E. F., and Beck, C. S. (1935). *Amer. Heart J.*, **10**, 293.
Kessler, H. H. (1941). *Accidental Injuries.* New Jersey, p. 387.
Kissane, R. W. (1937). *Contusion of the Heart.* Ohio State University, Columbus.
——, Fidler, R. S., and Koons, R. A. (1937). *Ann. intern. Med.*, **11**, 907.
—— —— —— (1940). *Advancement of Science*, **13**, 170.
Warburg, E. (1938). *Subacute and Chronic Pericardial and Myocardial Lesions due to Non-Penetrating Traumatic Injuries.* Copenhagen.
—— (1940). *Brit. Heart J.*, **2**, 271.
White, P. D., Chamberlain, F. L., and Graybiel, A. (1941). *Brit. Heart J.*, **3**, 233.
Zuckerman, S., Krohn, P. L., Whitteridge, D. (1942). *Lancet*, **1**, 252.

THE ELECTROCARDIOGRAM IN FRIEDREICH DISEASE

BY

WILLIAM EVANS AND GORDON WRIGHT

From the Cardiac Department of the London Hospital

Received May 5, 1942

It has been the custom to regard Friedreich disease as affecting only the central nervous system, but an examination of 38 cases has convinced us that the heart also is often affected.

When recording the clinical and pathological findings in a patient with Friedreich's ataxia who had been treated for heart failure at Guy's Hospital and the London Hospital, Newton Pitt (1887) said that not enough attention had been paid to the circulatory system in this disease: in his patient, heart failure had been an outstanding feature of the last phase of the fatal illness and was the cause of death. The case records of Friedreich disease published since deal chiefly with changes in the nervous system, and reference to symptoms connected with the heart has generally been either casual or missing. Yet a few cases that showed some abnormality of the heart have been recorded. Histological changes in the myocardium were described by Lannois and Porot (1905) and by Guizzetti (1933). Heart failure was reported by Omerod (1885) and Pitt (1887). Electrocardiographic irregularities have been described occasionally during the past ten years. Guillain and Mollaret (1932) found inversion of the T wave in leads II and III in one case, and a prolonged P–R interval with right axis deviation in another; so impressed were they by these changes that they spoke of the " cardiobulbar syndrome." Nodal arrhythmia, right electrical axis deviation, and a diphasic or inverted T wave in lead I were shown in an electrocardiogram published by Rathery, Mollaret, and Sterne (1934). Progressive cardiographic changes were watched for two years in a patient by Guillain and Mollaret (1934), and the last tracing showed inversion of T_2 and T_3. A similar curve was found in a child by Debré, Marie, Soulié, and de Font-Réaulx (1936). In eight patients examined by van Bogaert (1936) the cardiogram showed inversion of T_1 and T_2 in two cases and of T_2 and T_3 in another two; there were minor changes in two of the remaining four.

We became interested in the subject when a young woman (Case 1) suffering from this condition was found with Stokes-Adams attacks, and when we were told that her brother, similarly affected, had died at the age of 18 during an attack. We arranged to examine the heart specially in other cases of Friedreich disease, and in this paper we give the findings in 38 patients assembled for the

FIG. 1.—Female, aged 22 (Case 1). Complete and left bundle branch block with extrasystoles. Fig. 1, 2, and 3 have been reduced to 2/3.

investigation. In every case the diagnosis of the condition had been made by a neurologist, and a further routine examination was carried out before admitting the patient into the series. A limb lead electrocardiogram was recorded, and whenever an abnormality of the T wave showed in lead I, lead IVR was taken as well. Other chest leads were sometimes recorded. Cardioscopy was carried out in 34 patients, but not in 4 who were bedridden.

RESULTS

Clinical Examination of the Heart.—In only one patient (Case 1) was the pulse abnormal, and then it was slow from heart block and irregular from

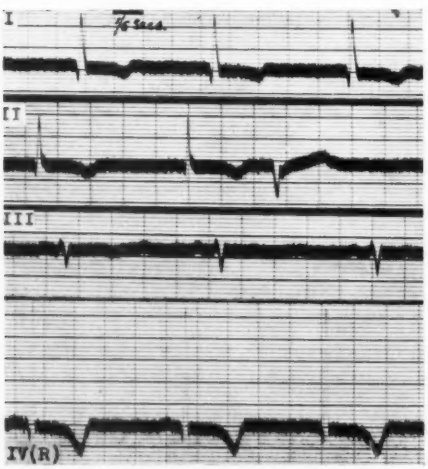


FIG. 2.—Male aged 50 (Case 2). T inverted in leads I, II, and IVR.

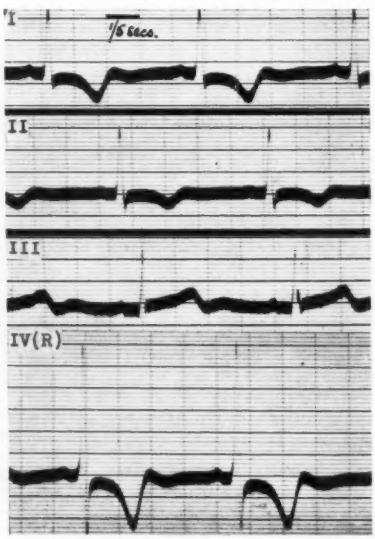


FIG. 3.—Male aged 22 (Case 3). T inverted in leads I, II, and IVR.

extrasystoles; the brother of this patient, who died in a Stokes-Adams attack at another hospital, is not included in this series because a cardiogram was not taken. None showed significant changes in blood pressure. The apex beat was often displaced outwards on account of scoliosis but not once from cardiac

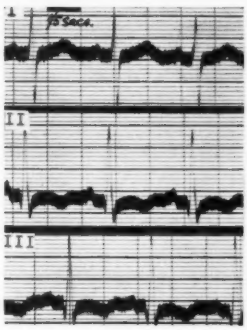


FIG. 4.—Female, aged 20 (Case 4). T inverted in leads II and III.

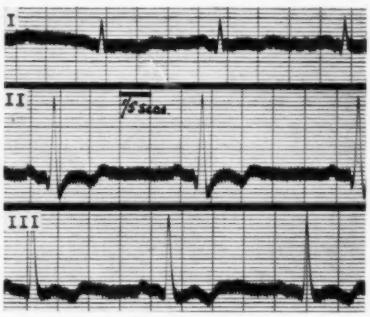


FIG. 5.—Male, aged 26 (Case 5). T low in lead I, and inverted in leads II and III.

hypertrophy. Noticeable murmurs were never found, and no valvular disease, either congenital or acquired. Except in four bedridden patients cardioscopy (i.e. radioscopy of the heart) was a routine method of examination, but it failed to demonstrate any gross changes; slight enlargement of the heart to the left,

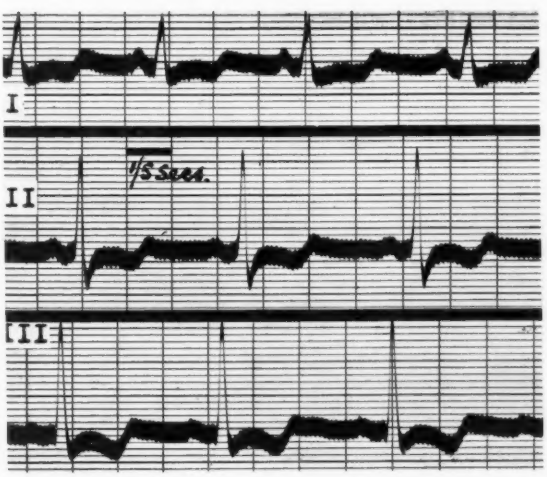


Fig. 6.—Female, aged 32 (Case 6). T wave inverted in leads I, II, and III.

sometimes confined to the toe of the left ventricle, was found in 8 patients, and 5 of these had prominent cardiographic changes.

Cardiographic Changes.—The electrocardiogram was abnormal in 12 of the 38 patients. In 10 others it was not strictly physiological, but these lesser

changes might have resulted from the deformity of the chest, which was a prominent feature of some of the cases.

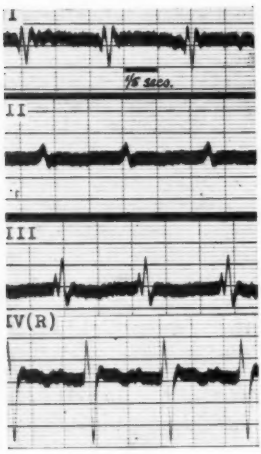


FIG. 7.—Male, aged 52 (Case 7). T flat in lead I, slightly inverted in leads II and III, and inverted in IVR.

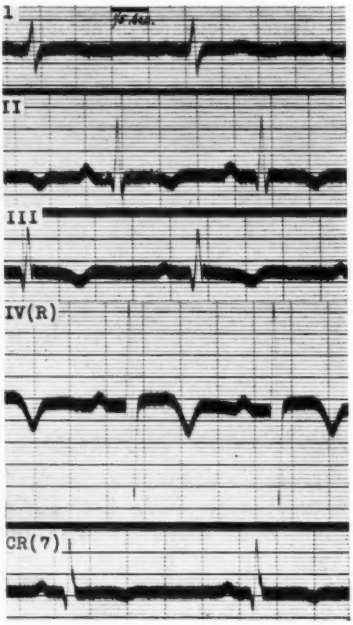


FIG. 8.—Male, aged 20 (Case 9). T just upright in lead I, inverted in leads II, III, IVR and CR_7.

Fig. 7–14 have been reduced to 7/8.

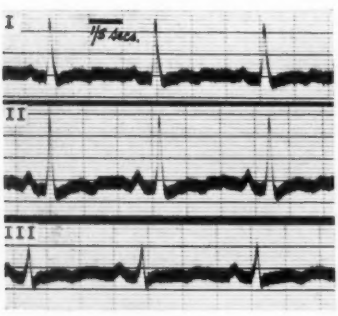


FIG. 9.—Female, aged 33 (Case 8). T inverted in leads I, II, and III.

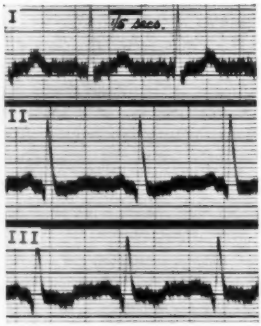


FIG. 10.—Female, aged 15 (Case 11). T just upright in lead II and diphasic in lead III.

Among the 12 abnormal cardiograms there was complete heart block and left bundle branch block in one (Fig. 1), inversion of the T wave conforming

to the T_1 type of cardiac infarction of Parkinson and Bedford (1927) in three (Fig. 2, 3, and 12), and to the T_3 type in three patients (Fig. 4, 10, and 11). In 5 cases (Fig. 5, 6, 7, 8, and 9) the T wave was low and usually inverted in all three limb leads.

In 5 of the 10 cases showing minor changes in the cardiogram the S wave

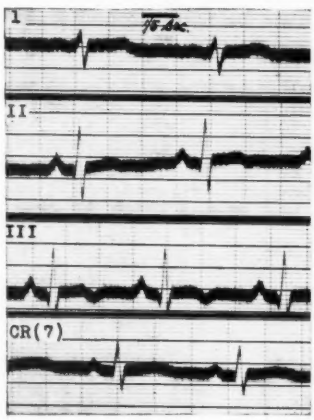


FIG. 11.—Male, aged 20 (Case 10). T inverted in lead III and just upright in leads I, II, and CR_7.

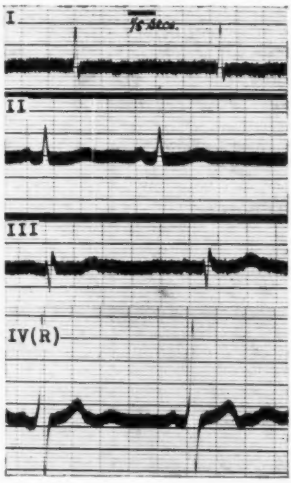


FIG. 12.—Male, aged 52 (Case 12). T inverted in lead I.

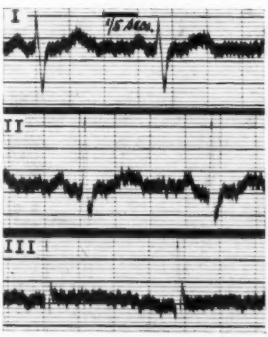


FIG. 13.—Female, aged 26 (Case 13). Deep and slurred S in leads I and II.

FIG. 14.—Male, aged 19 (Case 18). Deep S in leads II and III; deep Q in lead I.

was deep and often slurred in lead I and usually in lead II (Fig. 13), and in the remaining 5 there were corresponding changes in leads II and III (Fig. 14).

We did not expect to find any correlation between the incidence of cardiographic abnormalities and the distribution of lesions in the nervous system,

but it seemed worth while to inquire. The neurological findings were therefore tabulated in relation to the cardiographic changes in Table I, and more fully in Tables II, III, and IV at the end of the paper.

TABLE I

ABNORMAL SIGNS IN THE CENTRAL NERVOUS SYSTEM AND HEART IN 38 PATIENTS WITH FRIEDREICH DISEASE

Clinical Data	12 Patients with Prominent Cardiographic Changes	10 Patients with Lesser Cardiographic Changes	16 Patients with Normal Cardiograms
Family history	8 *	7	4 *
Ataxia and incoordination:			
Gross	5	8	8
Moderate	7	1	3
Slight	0	1	5
Speech affected	10 *	6	8 *
Nystagmus	7	8	12
Tremor	3	6	7
Absent Reflexes:			
Arm	7 *	5	3 *
Leg	11 *	8	9 *
Plantar Reflex:			
Extensor	11 *	4	8 *
Not determined	1	5	4
Flexor	0	1	4
Deformities:			
Pes cavus	10	9	11
Scoliosis	9	5	7

* Denotes a significant difference.

The incidence of cardiographic changes was in no way related to age or sex, or to the time of onset of the disease. Two neurological signs, absence of tendon reflexes, and extensor response of the plantar reflex, occurred in the patients with cardiographic irregularities so frequently as to be significant. Furthermore, reference to Table I shows that involvement of the nervous system as a whole was greatest in those with abnormal cardiograms.

The association of a family history of Friedreich disease with abnormal cardiographic changes was most striking. Thus 15 patients with abnormal cardiograms (gross changes in 8) had one or more relatives similarly affected, while only 4 with normal tracings had a family history. In this connection another feature came to light; that affected members of the one family tended to show the same cardiographic changes. The only patient in the series to show complete heart block and Stokes-Adams disease (Case 1), had a brother similarly affected. A sister and younger brother of Case 1 (Cases 17 and 18) showed comparable but lesser cardiographic changes. Another (Case 3), with inversion of T_1 and T_2, had a sister (Case 4) with inversion of T_2 and T_3. The cardiograms in a brother and sister (Cases 5 and 6) demonstrated inversion of T_2 and T_3. Twin brothers showed the same type of cardiographic changes although these were more severe in one (Case 9) than the other (Case 10). Two brothers and a sister (Cases 14, 15, and 16) exhibited similar tracings, but in two brothers (Cases 19 and 35) the curves were dissimilar. That identical physical

signs in relatives with Friedreich disease are not confined to the electrocardiogram was shown by two brothers (Cases 19 and 35) with primary optic atrophy, whose sister also was blind from birth and the subject of Friedreich disease.

The Meaning of the Cardiographic Findings

In the light of electrocardiographic changes in cardiac infarction it would be expected that the heart lesion in Friedreich disease usually lies in the muscle or in the conducting tissues. In those cases with a tracing similar to that found in cardiac infarction it is likely that the changes in the myocardium have a distribution in the anterior or posterior part of the heart, comparable with the areas involved when either the left or right coronary artery becomes occluded. In those patients with a " coronary type " of curve none so far have angina pectoris, and involvement of the coronary artery in Friedreich is unlikely. In a case with a cardiogram showing a Pardee type of curve, Laubry and de Balsac (1936) injected the coronary circulation with a mercurial preparation at necropsy, and in a subsequent radiogram they found no abnormality in the course of the coronary arteries. Our interpretation of the significance of the cardiographic changes also gains support from the histological findings in cases reported by Pitt (1887) and by Lannois and Porot (1905). Pitt described enlargement of the heart from hypertrophy of its walls and dilatation of its cavities. On microscopical examination he found that the muscle was healthy in many places; in some places it had undergone granular degeneration, and in others it had been replaced completely by loose and vascularized fibrous tissue, which in parts was crowded with small cells. D. S. Russell (1941) states that the heart in Friedreich disease may show a widespread change consisting of enlargement caused by thickening of the muscle and diffuse fibrosis; microscopical examination demonstrates fatty degeneration of the muscle fibres with slight chronic inflammatory infiltration and fibrosis.

It is not known yet whether the significant cardiographic changes predict the eventual onset of heart failure. Anyhow it is improbable that failure ever takes place in Friedreich disease when the electrocardiogram is normal, but the proximity of the event is likely to be judged best by the degree of cardiac enlargement determined by cardioscopy. The outlook is certainly ominous when the cardiogram signifies involvement of the bundle of His and especially when auriculo-ventricular dissociation has caused Stokes-Adams disease.

As a rule the diagnosis of Friedreich disease is straightforward after examination of the nervous system. When it is in doubt the electrocardiogram may help, for an abnormal tracing of the type described here supports the diagnosis although a normal curve does not exclude it.

Summary and Conclusions

The electrocardiogram in 38 patients with Friedreich disease was specially studied. This investigation has convinced us that the condition may sometimes be as much an affection of the heart as of the nervous system.

In only one patient, with Stokes-Adams disease, did clinical examination of the heart show any abnormality; in his case the pulse was slow from complete heart block and irregular from extrasystoles.

Cardiscopy, carried out in all except 4 bedridden patients, showed slight enlargement of the left ventricle in 8, and 5 of these had prominent cardiographic changes.

The cardiogram showed conspicuous or significant changes in 12 of the 38 patients. There were slight changes in another 10. In the remaining 16 the curve was physiological. In the first group 1 patient had complete heart block, 3 had a T_1 type of coronary curve, and 3 had a T_3 type of curve. In 5 the T wave was low and usually inverted in all three limb leads. In 5 of 10 patients showing lesser changes, the S wave was deep and slurred in lead I and usually in lead II, and similarly in leads II and III in the other 5 patients.

When the relation of abnormal signs in the nervous system to the cardiographic changes was examined, it was found that absence of tendon reflexes and extensor response of the plantar reflex were more common in patients with abnormal cardiograms. In respect of other nervous signs it may be said generally that they were more widespread in patients with the more conspicuous cardiographic changes. Of greater significance appeared to be the high incidence of a family history of Friedreich disease in those showing cardiographic changes. Thus 15 out of 22 patients with abnormal cardiograms (8 of them showing gross changes) had one or more relatives, usually a brother or sister, similarly affected, while only 4 out of 16 patients with normal curves provided this family history. The affected members of the same family tended to show identical cardiographic changes.

The electrocardiogram may help to establish the diagnosis of Friedreich disease when the neurological manifestations are not altogether typical of the condition; an abnormal tracing lends support to the diagnosis, but a normal curve does not exclude it. In prognosis too the cardiogram can be of assistance; when it proves involvement of the bundle of His it may foretell auriculo-ventricular dissociation and Stokes-Adams disease with its ominous outlook. The exact significance of a " coronary type " of curve is not known yet, but it is probable that only such cases are prone to develop heart failure, although the proximity of this event may be more closely related to the degree of cardiac enlargement, which is best determined by cardioscopy.

For these reasons we would say that the investigation of a patient with Friedreich disease is incomplete without electrocardiography and cardioscopy.

We are grateful to Dr. A. Hunter, First Assistant to the Department, who helped us in many ways, and to the following who assisted us in the collection of cases: Dr. W. R. Brain, Dr. A. E. Clark-Kennedy, Dr. C. Ellingworth, Dr. A. Feiling, Dr. A. R. Gilchrist, Dr. L. J. Grant, Dr. W. Harris, Dr. N. G. Hulbert, Dr. D. Hunter, Dr. R. Kempthorne, Mr. I. Lewis, Dr. R. Mackay, Dr. J. McM. Mennell, Mr. A. M. A. Moore, Dr. E. A. B. Pritchard, Dr. B. Russell, Dr. E. M. Sawdon, Dr. P. H. S. Shaw, Dr. B. Varling, and Dr. M. W. Warren.

We wish to thank Dr. John Parkinson, Physician to the Cardiac Department, for his helpful criticism of this paper.

References

van Bogaert, A. and L. (1936). *Arch. Mal. Cœur*, **29,** 630.
Debré, R., Marie, J., Soulié, P., and de Font-Réaulx, P. (1936). *Bull. Mém. Soc. méd. Hôp., Paris*, **52,** 749.
Guillain, G., and Mollaret, P. (1932). *Presse Méd.*, **40,** 1621.
—— —— (1934). *Bull. Mém. Soc. méd. Hôp., Paris*, **50,** 1577.
Guizzetti, P. (1933). *Riv. Patol. Nerv.*, **41,** 545.
Lannois, M., and Porot, A. (1905). *Rev. méd., Paris*, **25,** 853.
Laubry, C., and de Balsac, R. H. (1936). *Bull. Mém. Soc. méd. Hôp., Paris*, **52,** 756.
Ormerod, J. A. (1885). *Brain*, **7,** 105.
Parkinson, J., and Bedford, D. E. (1927). *Heart*, **14,** 195.
Pitt, G. N. (1887). *Guy's Hosp. Rep.*, **44,** 369.
Rathery, F., Mollaret, P., and Sterne, J. (1934). *Bull. Mém. Soc. méd. Hôp., Paris*, **50,** 1382.
Russell, D. S. (1941). Personal communication.

Notes of the 38 cases are given in Tables II, III and IV on pages 100 to 102.

TABLE II

TWELVE PATIENTS SHOWING SIGNIFICANT OR PROMINENT CARDIOGRAPHIC CHANGES

Case No.	Sex	Age	Relatives with Friedreich Disease	Age at Onset of Symptoms	Ataxia and Incoordination	Speech Affected	Nystagmus	Tremor	Reflexes			Deformities		Cardioscopy	Cardiographic Changes
									Arm	Knee and Ankle	Plantar	Pes Cavus	Scoliosis		
1	F	22	2 brothers and sister (Cases 17 and 18)	11	++	+	+	−	−	−	Extensor	+	+	L.V. slightly+	Complete heart block with extrasystoles; left bundle branch block
2	M	50	None	16	++	+	−	−	+	−	Extensor	+	−	−	T_1 and T_2 inverted as well as T in IVR
3	M	22	Sister (Case 4)	14	++	+	−	−	+	−	Extensor	+	+	−	do.
4	F	20	Brother (Case 3)	18	+	+	−	−	−	−	Extensor	+	−	Normal	T_2 and T_3 inverted
5	M	26	Sister (Case 6)	13	+	+	+	+	−	−	Extensor	+	+	L.V. slightly+	do.
6	F	32	Brother (Case 5)	12	+	+	+	+	−	−	Extensor	+	+	Normal	T_1, T_2, and T_3 inverted
7	M	52	None	27	++	+	+	−	+	−	Extensor	+	+	L.V. slightly+	T_1 flat, T_2 and T_3 slightly inverted, and T inverted in IVR
8	F	33	Brother	13	+	+	−	−	+	−	Extensor	+	+	Normal	T_1, T_2, and T_3 inverted
9	M	20	Brother (Case 10)	16	+	−	+	−	−	−	Extensor	+	+	L.V. slightly+	T_2 and T_3 inverted: T_1 just upright. T inverted in IVR and CR_7
10	M	20	Brother (Case 9)	16	++	+	+	+	−	−	Extensor	−	+	Normal	T_3 inverted and T just upright in II and CR_7; deep S_1
11	F	15	None	10	+	−	−	−	−	−	Indefinite	+	−	Normal	T diphasic in III and just up in II
12	M	52	None	11	+	+	+	−	+	+	Extensor	−	+	L.V. slightly+	T_1 inverted

TABLE III

TEN PATIENTS SHOWING LESSER CARDIOGRAPHIC CHANGES

Case No.	Sex	Age	Relatives with Friedreich Disease	Age at Onset of Symptoms	Ataxia and Incoordination	Speech Affected	Nystagmus	Tremor	Reflexes			Deformities		Cardioscopy	Cardiographic Changes
									Arm	Knee and Ankle	Plantar	Pes Cavus	Scoliosis		
13	F	26	None	11	+	−	+	−	+	+	Indefinite	+	−	Normal	Deep and slurred S_1 and S_2
14	F	44	2 brothers (Cases 15 and 16)	18	++	+	+	+	−	−	Indefinite	+	−	Normal	Deep and slurred S_1, S_2, and S_3
15	M	34	Sister and brother (Cases 14 and 16)	18	++	+	+	+	+	−	Indefinite	+	−	Normal	Deep and slurred S_1
16	M	42	Sister and brother (Cases 14 and 15)	19	++	+	+	+	−	−	Indefinite	+	+	Normal	do.
17	F	15	Sister and 2 brothers (Cases 1 and 18)	10	++	+	+	+	−	−	Extensor	+	+	Normal	do.
18	M	19	2 sisters (Cases 1 and 17) and brother	12	++	+	+	—	−	−	Flexor	+	+	L.V. slightly +	Deep S_2 and S_3; deep Q_1
19	M	43	Brother (Case 35) and sister	Infancy	++	−	−	+	+	+	Extensor	+	−	Normal	Deep and slurred S_1, S_2, and S_3
20	M	39	None	15	++	−	−	−	−	−	Indefinite	+	+	Normal	Deep S_2 and S_3
21	M	16	None	8	++	Dumb	+	−	+	−	Extensor	+	−	—	do.
22	M	45	4 brothers	34	+	+	+	+	+	−	Extensor	−	+	Normal	do.

TABLE IV

16 PATIENTS WITH NORMAL CARDIOGRAM

Case No.	Sex	Age	Relatives with Friedreich Disease	Age at Onset of Symptoms	Ataxia and Incoordination	Speech Affected	Nystagmus	Tremor	Reflexes			Deformities		Cardioscopy
									Arm	Knee and Ankle	Plantar	Pes Cavus	Scoliosis	
23	M	21	None	11	++	Dumb	+	−	+	−	Flexor	−	+	Normal
24	M	39	None	23	++	+	+	+	+	−	Flexor	−	+	Normal
25	F	36	None	11	++	+	+	+	+	−	Flexor	−	+	Normal
26	F	37	None	15	++	+	+	+	+	+	Extensor	+	+	Normal
27	M	13	None	12	+	−	+	−	+	+	Extensor	+	−	Normal
28	M	56	None	12	++	+	+	−	+	+	Extensor	+	−	−
29	F	32	None	11	++	+	+	+	+	−	Extensor	−	+	Normal
30	F	21	None	10	+	−	−	−	+	−	Flexor	+	−	L.V. slightly+
31	F	19	Sister (Case 36)	7	+	−	+	−	+	+	Extensor	+	−	Normal
32	M	45	None	23	+	−	−	+	−	−	Indefinite	+	−	Normal
33	F	30	None	17	+	−	+	−	+	−	Indefinite	+	−	L.V. slightly+
34	M	22	None	14	+	−	+	−	+	+	Extensor	+	−	Normal
35	M	48	Brother (Case 19) and sister	Infancy	++	−	−	+	+	+	Extensor	+	−	Normal
36	F	34	Sister (Case 31)	13	++	−	−	+	+	+	Indefinite	−	+	Normal
37	F	26	None	18	+	+	+	−	−	−	Extensor	+	+	Normal
38	M	31	Uncle	16	+	+	+	−	−	−	Indefinite	+	−	Normal

INTRACARDIAC TUMOURS

BY

J. L. HAMILTON-PATERSON AND L. I. M. CASTLEDEN

From the Redhill County Hospital, Edgware, Middlesex

Received June 1, 1942

Three cases of intracardiac tumour are reported in this paper and are of interest, apart from the comparative rarity of the condition, because in each case the clinical signs and symptoms suggested the presence of another lesion and the tumour was only discovered post-mortem.

The first case, with a round-cell and spindle-cell sarcoma of the right auricle, showed in life the signs and symptoms of Ayerza's syndrome. The second, with a pedunculated myxomatous tumour of the left auricle, which projected through the mitral valve, was diagnosed as mitral stenosis. The third, with a tumour only in the sense that it was an intracardiac swelling, had a mycotic aneurysm arising at the attachment of the anterior cusp of the aortic valve, extending downwards into the interventricular septum and bulging into the right ventricle; the aortic valve was the seat of a bacterial endocarditis: in life the bulging into the right ventricle had obstructed the pulmonary valve, and a diagnosis of pulmonary stenosis and rheumatic carditis had been made.

Sarcoma of Right Auricle

Case 1. A woman, aged 45 years, was admitted 30/7/41 complaining of increasing shortness of breath on exertion, of blueness of the lips for five months, and of a cough with scanty sputum for the past four weeks. Her doctor stated that auricular fibrillation had developed within the last week. She had always been strong and healthy except for a tendency to winter cough for the past five or six years. No history of rheumatic fever or chorea.

On examination she was an obese woman with intense plum-coloured cyanosis but without dyspnœa at rest. The heart appeared normal in size. Auricular fibrillation at 84 a minute was present. There were no murmurs. The blood pressure was 120/80. The lungs were emphysematous without any added sounds. The cervical veins were not overfilled, and there was no œdema of the subcutaneous tissues and no enlargement of the liver or spleen. The appearance of the patient suggested polycythæmia, but her blood count showed 4·7 million red blood corpuscules and 94 per cent hæmoglolin, with a colour index of 1·0. The urine was normal except for a trace of albumin. An electrocardiogram confirmed the presence of auricular fibrillation and showed low voltage of the QRS complexes and a flat T wave in lead III. There was no abnormal axis deviation.

On 6/8/41 the right leg suddenly became swollen up to the groin, painful,

œdematous, and more blue than the left. Physical examination showed no other change. The white blood corpuscles were 7000 per c.mm., with neutrophils 73 per cent, lymphocytes 15 per cent, monocytes 10 per cent, and eosinophils 2 per cent. On 11/8/41 there were a few râles at the right base, and thereafter signs of congestive failure increased until on 17/8/41 there were bilateral pleural effusions with œdema of both legs up to the groins. The right leg, which had remained swollen since the onset of the venous thrombosis, was still more œdematous. The heart appeared to be enlarged to the left and fibrillation was still present at 88 a minute. Mersalyl produced a severe reaction and was discontinued. Other efforts to relieve her congestion failed and sacral œdema appeared. On 25/8/41 the heart was still enlarged but the rhythm now became regular, the blood pressure remaining at 120/80. A cardiogram confirmed the presence of regular rhythm at 84 a minute, with a P–R interval of 0·28 sec. The QRS complexes still showed a low voltage with normal R–T intervals. The T waves in leads I and II were upright but flat in lead III.

The patient remained very ill with no change in her congestive failure, and on 30/8/41 venous thrombosis occurred in the right arm, which was œdematous up to the shoulder. Œdema of the right breast developed. Acupuncture of both feet was performed; the punctures drained about three pints a day and all the œdema, except that of the right arm, disappeared. The cyanosis, however, which had remained a marked feature throughout, became more intense, and for the first time she began to be dyspnœic at rest in bed. The Wassermann, Kahn, and Laughlen reactions were negative, and an X-ray of her chest showed an abnormal heart shadow with considerable bulging to the right, the appearance being consistent with pulmonary stenosis. The patient was too ill to be screened. Œdema now began to increase again, and on 12/10/41 venous thrombosis occurred in the left arm. From this point the patient's condition steadily deteriorated. Slow auricular fibrillation at 90 a minute recommenced, the cervical veins became overfilled and the œdema progressed to a generalized anasarca with intense cyanosis, which persisted until death on 22/11/41.

Post-mortem Examination. Heart weight 600 g. Parietal pericardium normal. There was a blood-stained pericardial effusion of about 4 oz. The heart was enlarged and grossly distorted by a lobulated tumour growing in the right auricle. When the right side of the heart was opened the whole auricle was filled with large nodules of growth all arising from the auricular wall which was itself thickened with growth (Fig. 1). The tumour was soft and white in colour, but in places there were large hæmorrhages into it. Auricular cavity, almost completely occluded by growth. Right and left ventricles and left auricle, normal except for some distortion caused by pressure of the enlarged right auricle. Pulmonary artery, normal. One nodule of tumour had grown through the inter-auricular wall and was presenting as a red mass in the left auricle about half an inch in diameter. The right coronary vein appeared to be completely occluded by growth. The superior vena cava was filled with clot, which, on dissection, was found to consist of several clots separately attached to the wall of the vein and joined together by post-mortem thrombus.

FIG. 1.—Case 1. Heart showing lobulated tumour filling right auricle.

The coronary arteries and aorta were normal. There were small ante-mortem thromboses in both femoral arteries immediately below the inguinal ligament.

Sections.—Heart: cellular growth invading myocardium (Fig. 2). Cells large and mostly round, with scanty eosinophilic cytoplasm. Some strands of

spindle-shaped cells were present. Nuclei, oval or round, with fine chromatin network. There were one or two areas with very large cells with giant nuclei. No true giant cells seen. Sections stained by Van Gieson showed no fibrous tissue. In many sections, stained with Mallory's phosphotungstic acid hæma-

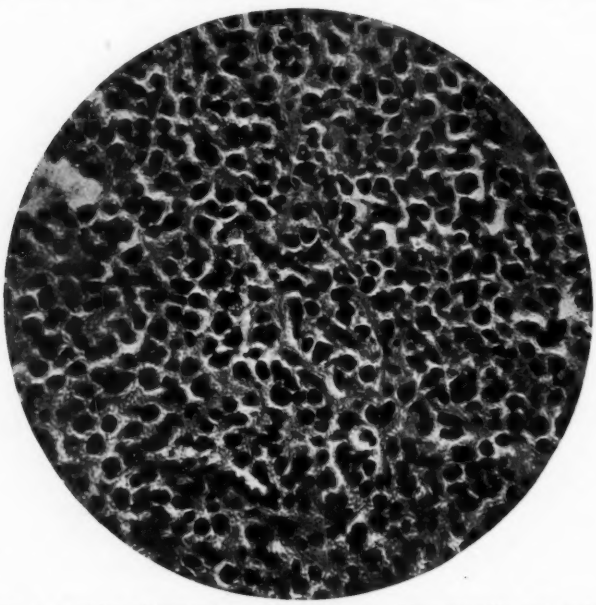


FIG. 2.—Case 1. Section of tumour showing structure. Hæmatoxylin and eosin. Magnification × 350.

toxylin and Heidenhain's iron hæmatoxylin, no cross striation demonstrated in the cells. No evidence of secondary growth in sections of the thromboses in the femoral arteries.

PSEUDO-MYXOMA OF LEFT AURICLE

Case 2. A man, aged 46 years, was admitted with a history of cardiac trouble since the age of 15 when he had influenza. He was always rather short of breath but was able to work until ten days ago when he became increasingly weak and breathless and vomited frequently. He had been treated for gastric symptoms between January and August, 1940, but otherwise had been well in the past apart from a gunshot wound in the neck in the last war. On admission he was extremely blue and dyspnœic with tense neck veins. Cold extremities. No œdema. Pulse 79, weak but regular. Blood pressure not registered (systolic below 90). Heart: grossly enlarged to left; loud apical systolic murmur. Lungs: congestion of both bases, more marked on the right. Abdomen: liver enlarged, almost to umbilicus, and tender. He died two days after admission.

Post-mortem Examination. Heart weight 750 g., grossly enlarged. Peri-

cardium and pericardial cavity normal. There was some hypertrophy of the right ventricle, which was filled with post-mortem clot. The tricuspid valve and the pulmonary valve were normal. Left auricle filled with a large pedunculated yellowish mass which had a short process projecting through the mitral valve into the left ventricular cavity. This mass was attached firmly to the middle wall of the left auricle over an area of about an inch in diameter (Fig. 3).

FIG. 3.—Case 2. Heart showing pedunculated tumour in left auricle.

The mass itself was solid in the lower part, but in the upper part was composed of small attached grape-like structures, which, on section, appeared to be myxomatous. Section of the solid parts showed structure partly laminated, partly hæmorrhagic, and partly amorphous. There was a small process, which was calcified, attached to the part projecting through the mitral valve. The mitral and the aortic valves and the coronary arteries were normal.

Sections.—Composed chiefly of structureless or fibrillary eosinophilic material in which were isolated groups and chords of cells (Fig. 4). In places these cells were flattened, and lined spaces which usually were filled with red

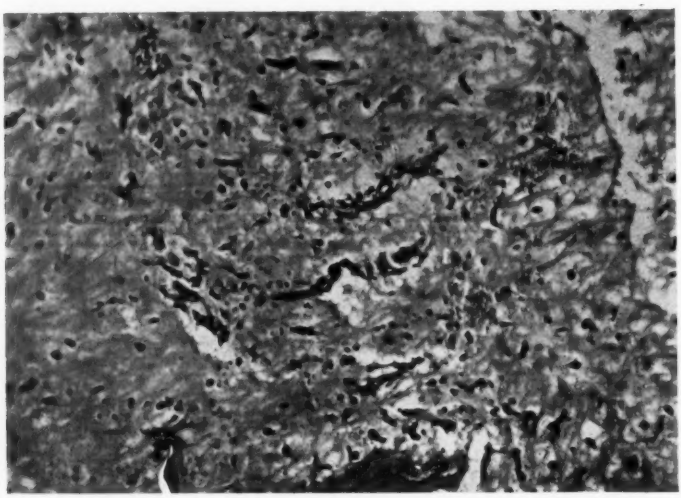


FIG. 4.—Case 2. Section of tumour showing general structure. Hæmatoxylin and eosin. Magnification × 120.

cells. Elsewhere the cells were rounded and had more cytoplasm and generally appeared like swollen connective tissue cells (Fig. 5). There was much iron containing pigment showing a perivascular distribution. Sections stained with thionin showed mucoid degeneration scattered irregularly through the sections.

MYCOTIC ANEURYSM SIMULATING PULMONARY STENOSIS

Case 3. A man, aged 25 years, was admitted on 31/12/41. He had always been quite well until eight months before when he was in a Shropshire hospital for six weeks with rheumatic fever. Shortly after his discharge he was passed fit for military service, " slight heart disease " being noted at the time. Two months later he was re-examined and said to be " cured." Four months before he had been discharged from the army on account of his heart. Six weeks before he had began to have aching in arm and leg joints without swelling, and was treated at home for rheumatic fever. At the same time he began to be short of breath, this symptom steadily increasing up to his admission. He also complained of thirst and had passed less urine than usual. For three days there had been

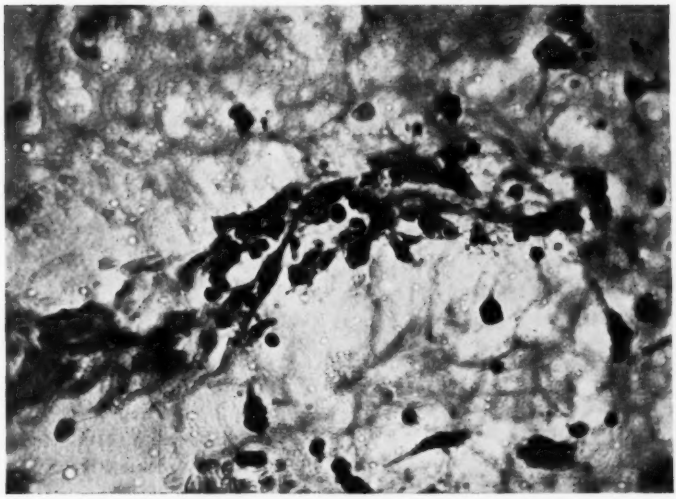


FIG. 5.—Case 2. Showing a cord of swollen connective tissue cells. Hæmatoxylin and eosin. Magnification × 350.

puffiness of his eyelids with slight headache. On admission he was wasted, with clubbing of the fingers, cyanosis, and dyspnœa, but was able to lie flat. There was puffiness of the eyelids, but no other peripheral œdema. The heart was enlarged to the left, the apex beat being almost out to the anterior axillary line in the fifth space, with a regular tachycardia at 138. Systolic and diastolic murmurs were present at both the mitral and aortic areas. There was a loud rough systolic murmur at the pulmonary area, which was conducted upwards and outwards to the left. A thrill was not felt. The blood pressure was 150/90. The lungs were normal. In the abdomen the liver edge was three inches below the costal margin and was smooth and tender. The spleen was just palpable. There was no ascites. No petechiæ were seen. A diagnosis of pulmonary stenosis with super-added infective endocarditis and perhaps rheumatic carditis was made. The patient died a few hours after admission.

Post-mortem Examination. Heart weight 630 g. Pericardium normal, but a pericardial effusion of about 6 oz. of clear yellow fluid. Both ventricles hypertrophied, particularly the left. Myocardium, pale in colour but not friable. Mitral valve, normal in every respect; no change found in the left auricle. Aortic valve, completely disorganized, cusps adherent and calcified with numerous small beady vegetations all over their surfaces. The orifice of the aortic valve was irregular and nowhere more than one-eighth of an inch diameter. The extreme fibrosis and calcification of the aortic valve had caused distortion of the sinus of Valsalva, and the orifices of the coronary arteries were completely pulled out of place. The anterior wall of the aorta, between the origin of the right coronary artery and aortic cusps, was infected and had given way to form a mycotic aneurysm pushing downwards in the interventricular wall. The cusps of the pulmonary valve were stretched over

the anterior wall of the aneurysm and very much distorted. The aneurysm projected into the right ventricular cavity and gave the appearance of a smooth rounded tumour (Fig. 6). The aorta itself was narrowed, but when it was

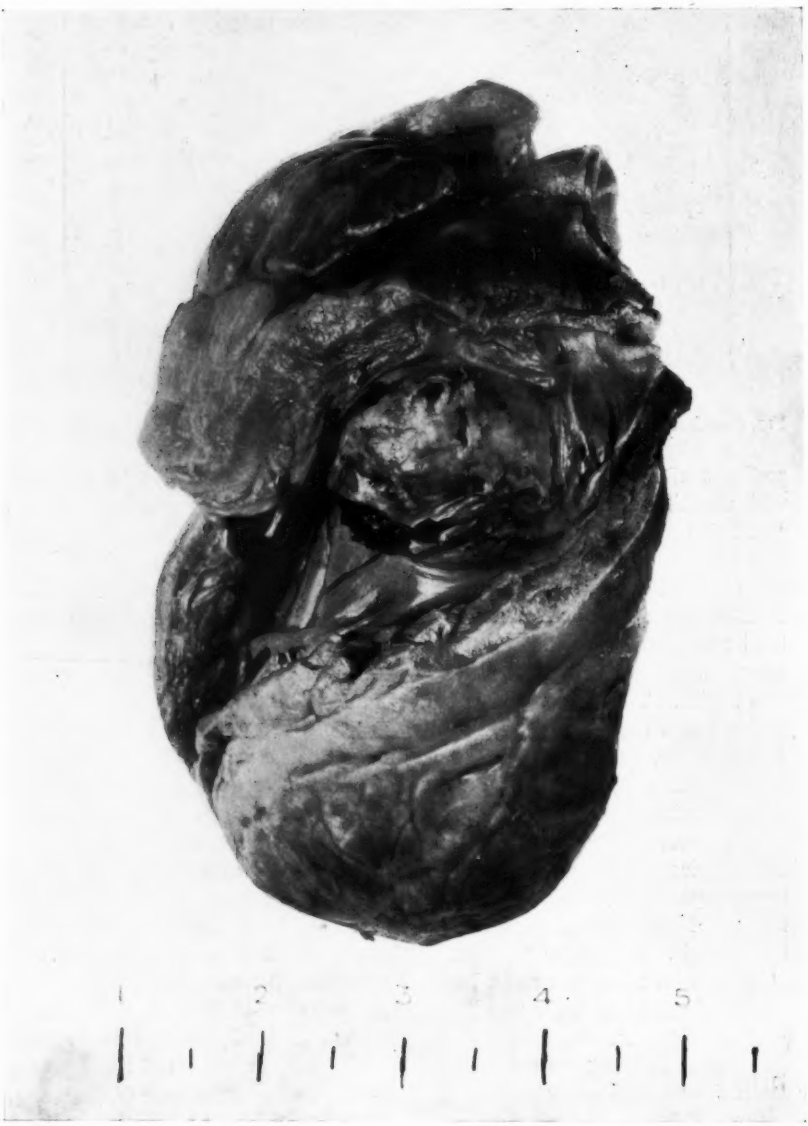


FIG. 6.—Case 3. Showing projection of the aneurysm into the right ventricle with distortion of the cusps of pulmonary valve.

opened there was no evidence of atherosclerosis. The distortion of the aortic valve was so great that it was impossible to tell whether it was tricuspid or not. The cavity of the aneurysm was lined by a smooth, shining membrane. In the wall of the left ventricle, at the root of the aorta, there was a cavity about one inch long and half an inch in diameter, filled with creamy blood-stained material. This was apparently an abscess in the myocardium extending directly from the infected anterior cusp of the aortic valve. The cavity of the right ventricle, apart from the distortion caused by the aneurysm, showed no abnormality. The tricuspid valve and the right auricle were normal. There was no occlusion of the coronary arteries.

Sections.—The wall of the aneurysm showed organizing and infected blood clot. The myocardium contained many free cells, macrophages, and polymorphs. There were some perivascular collections of macrophages suggesting the formation of Aschoff bodies.

Discussion

Clinical.—Intracardiac tumour is seldom suspected and less often diagnosed because of the rarity of the lesion and the absence of characteristic signs and symptoms. In adults the commonest findings are those of congestive cardiac failure and cardiac enlargement with or without murmurs suggesting valvular lesions. There may, however, be no signs or symptoms referable to the heart (Bradley and Maxwell, 1928). Other symptoms recorded have been cough, hæmoptysis, weakness, attacks of fainting, præcordial pain, abdominal pain, headache, and vomiting. Œdema is usually general, but may be confined to the face, neck, upper arm, and thorax, suggesting occlusion of the superior vena cava. Various pulse abnormalities have been described, and in two cases there was heart block. Pleural and pericardial effusions often occur and may be hæmorrhagic. The malignant tumours may give rise to secondary growths, presumably blood borne, in the lung, pancreas, intestine, etc. (Muller, 1932).

In fact, the presence of a tumour in the walls or cavities of the heart may simulate all kinds of cardiac disease, and such diagnostic criteria as one can formulate must lie in the very multiplicity of the signs. These may be such that they suggest two separate lesions that are unlikely to occur together, and the presence of even one markedly anomalous sign perhaps should lead one to include "tumour" in the differential diagnosis. In children, of course, the natural diagnosis has been congenital morbus cordis (Farber, 1931), but signs of cerebral sclerosis or other congenital abnormality should lead one to suspect rhabdomyoma of the heart, as this occurs in a large percentage of cases of tuberose sclerosis.

Case 3 particularly shows anomalous features. The signs were those of pulmonary stenosis of marked degree with probably old rheumatic lesions of the aortic and mitral valves and an added infective endocarditis. Pulmonary stenosis is usually congenital, but in this case it had not been discovered at his several previous medical examinations and must have developed within two or three months. The changing nature of the signs recorded by the medical board were in favour of the infective nature of the lesion. Although these

features raised doubts as to the nature of the valvular lesion, further study would probably not have led to an accurate diagnosis of the condition found post-mortem. In Case 1 the successive diagnoses had to be discarded for lack of confirmatory evidence. At the first examination she appeared to be a case of primary polycythæmia, but this could not be supported in face of the blood count. No evidence of syphilis could be found to corroborate a diagnosis of Ayerza's disease, and the lungs were comparatively clear. The peripheral thromboses were insufficient to account for the intense cyanosis. Such a degree of cyanosis should have been accompanied by secondary polycythæmia, or by the early appearance of right heart failure with congestion, or both. However, none of these conditions obtained until the patient was moribund. Had the patient been well enough to have been screened, the gross enlargement of the right auricle might have been demonstrated, and this, in conjunction with the physical signs, might have led to a correct diagnosis. In Case 2, the clinical appearances were those of a single rheumatic lesion of the mitral valve without a definite history of rheumatism. This does occur in both sexes of course, but is more common in females. A similar tumour, arising from the aortic valve and causing sudden death was described by Campbell and Carling (1934).

Pathological.—The chief interest lies in the pseudo-myxoma described in the second case. Nearly 200 primary heart tumours have been described and about half of these fall into the pseudo-myxoma group. The study of their histological features has resulted in two theories relating to their origin. Thorel (1903) and, more recently, Fawcett and Ward (1939) thought they were pedunculated thrombi, which, during the process of organization, underwent a mucoid degeneration that gave rise to their myxomatous appearance. Other observers contend that the tumours are primarily new growths, and each has given them names according to their variations in structure. Thus Rau (1898), Manifold (1915), and Schuster (1914) described cavernous angiomata; Hornowski (1906) and Orr (1942) described endotheliomata; Lloyd (1929) and Armstrong and Monckeburg (1911) described lymphangio-endotheliomata; Fabris (1923) described a fibro-angio-myxoma, and Brenner (1907) a hæmangio-elasto-myxoma. The basic histological structure tends to be constant in all these tumours, and difference of opinion as to their ætiology has arisen from different interpretations of the observed features. The various elements may be present in different proportions giving rise to rather widely varying pictures, but in all cases the matrix of the tumour is the structureless pseudo-myxomatous material. In this are spaces lined by endothelium, which may be large enough to resemble sinuses or as small as capillaries, and all intermediate stages are met with. If the sinus-like spaces predominate, the appearance of angioma is simulated. If instead of spaces, the cells are in rows or columns the appearance is that of an endothelioma. In our case these columns rarely contained more than two rows of cells and looked like strands of young connective tissue growing into the stroma. Scattered throughout the sections, often ranged perivascularly, are areas showing large or small masses of iron containing pigment.

Most observers are agreed that the mucoid tissue is the result of degeneration, but the presence of mucin has been said to denote the epithelial origin of

a tumour, although in these cases the only possible source of mucin would be the lining cells of the vascular spaces; perivascular distribution of the mucin in some of the tumours has been cited in favour of this. The presence of iron is said by some to be due to the breaking down of blood in the thrombus and by others to have resulted from hæmorrhage into the tumour, particularly in the angiomatous types. Elastic fibres have also been described and put forward as evidence of new growth, but Muller (1932) points out that they may occur in well-organized thrombi. The cellular elements have been regarded as neoplastic because in some cases they appear to reproduce differentiated structures such as blood and lymph sinuses, and sometimes appear hyperplastic, i.e. they may be swollen and contain one or two nuclei or may be built up into two or more layers. All these appearances, however, may be met with when young connective tissue cells invade blood clot during the process of organization. We have recently seen a case of mitral stenosis that showed a large plaque-like mass of organizing thrombus adherent to the medial wall of the left auricle, which histologically showed all the above features except that elastic tissue was absent. It would seem, therefore, that organizing thrombus can produce the picture called pseudo-myxoma, and in the absence of definite features, which could be ascribed only to a neoplasm, i.e. the presence of tumour tissue in the heart wall itself, it is reasonable to suppose that they are organizing thrombi.

These tumours usually occur in the left auricle and are often attached in the region of the scar of the foramen ovale. Meroz (1917) collected 40 reports of primary intracardiac tumour, 30 of which were in the left auricle. The surface of the tumours may either be smooth, as in our case, or have a granular appearance. On section the cut surface looks translucent and mucoid, and the outer layers may be composed of laminated blood clot.

Case 1 is a true sarcoma, composed of round and spindle cells. Bradley and Maxwell (1928) have classified 36 cases of primary sarcoma of the heart; 12 were spindle-cell, 10 round-cell, 4 giant-cell growths, 3 myxosarcomatous, and 1 each lymphosarcomatous and angiosarcomatous. These tumours are known to metastasize as in two cases reported by Muller (1932), one with a secondary nodule in the lung, and the other with secondary nodules in the lung, pancreas, and small intestine. This latter case and the case first reported by Bradley and Maxwell (1928) were examples of rhabdomyosarcomata with demonstrable cross striation in some of the tumour cells.

There is yet a third main group of intracardiac tumours, the congenital rhabdomyomata. These are composed of cells similar to embryonic heart muscle (" spider cells "), are often associated with tuberose sclerosis; they are never malignant and often multiple.

From our survey of the reported cases, it would appear that all the cases can be placed into one of the three main groups discussed: i.e.:—

(1) the pseudomyxomata, which for reasons already explained are probably not true tumours but organized thrombi,

(2) the true sarcomata, which may arise from any of the mesenchymal elements in the heart wall, and

(3) the congenital rhabdomyomata (dysontogenetic rhabdomyoma, hamartoma).

The pseudomyxomata form the largest group and comprise nearly half of the tumours described. One quarter of the cases fall into the class of primary sarcoma. Beck and Thatcher (1925) commented on thirty-three reported cases and added one of their own. Nowicki (1926) reported four cases, Matras (1927) one case, and Bradley and Maxwell (1928) and Muller (1932) added one and two cases respectively. The remaining 25 per cent of the cases belong to the category of congenital rhabdomyoma. Farber (1931) found forty-one cases reported, and since then we have only come across two more cases, one described by Ill and Gray (1941) and one by Stewart (1939).

Summary

Three cases of intracardiac tumour are described, a sarcoma, a " pseudomyxoma," and an aneurysm; which in life produced signs and symptoms attributable to Ayerza's syndrome, mitral stenosis, and pulmonary stenosis respectively.

The origin of pseudomyxomata of the heart is discussed. It is suggested that they are not primarily neoplastic but are pedunculated thrombi as all their histological features may be reproduced in organizing blood clots.

A classification of heart tumours is suggested:

(1) Benign tumours resulting from organization of blood clot—pseudomyxomata,

(2) Malignant tumours arising from any of the mesenchymal elements of the heart wall, the true sarcomata, and

(3) Benign congenital tumours arising from developing myocardial elements, the congenital rhabdomyomata (dysontogenetic rhabdomyoma, hamartoma).

Dr. G. H. Jennings kindly gave us permission to publish the clinical details of Case 2. The photographs were taken by Mr. H. D. J. Cole.

References

Armstrong, H., and Monckeburg, J. G. (1911). *Dtsch. Arch. klin. Med.*, **102,** 144.
Beck, C. S., and Thatcher, H. S. (1925). *Arch. intern. Med.*, **36,** 830.
Bradley, E. B., and Maxwell, F. S. (1928). *J. Amer. med. Ass.*, **91,** 1352.
Brenner, F. (1907). *Frankf. Z. Path.*, **1, 492.**
Campbell, M., and Carling, W. R. (1934). *Guy's Hospital Reports*, **84,** 41.
Fabris, A. (1923). *Arch. Path. Anat.*, **241,** 59.
Farber, S. (1931). *Amer. J. Path.*, **7,** 105.
Fawcett, R. E. M., and Ward, E. M. (1939). *Brit. Heart J.*, **1,** 249.
Hornowski, J. (1906). *Zbl. Allg. Path.*, **17,** 773.
Ill, C. H., and Gray, J. W. (1934). *Amer. J. Obstet. Gynaetc.*, **28,** 265.
Lloyd, P. C. (1929). *Bull. Johns Hopkins Hosp.*, **44,** 149.
Manifold, R. F. (1915). *Lancet*, **2,** 1027.
Matras, A. (1927). *Z. H. Kreisslaufforsch.*, **19,** 233
Meroz, E. (1917). *Internat. Clin.*, **4,** 231.
Muller, W. (1932). *Virchow's Arch.*, **284,** 105.
Nowicki, W. (1926). *Virchow's Arch.*, **259,** 502.
Orr, J. W. (1942). *J. Path. Bact.*, **54,** 125.
Rau, F. (1898). *Arch. Path. Anat.*, **153,** 22.
Schuster, H. (1914). *Arch. Path. Anat.*, **215,** 335.
Stewart, T. D. (1939). *N. Zealand med. J.*, **38,** 19.
Thorel, C. (1903). *Ergebn. Allg. Path.*, **91,** 901.

GRAHAM STEELL

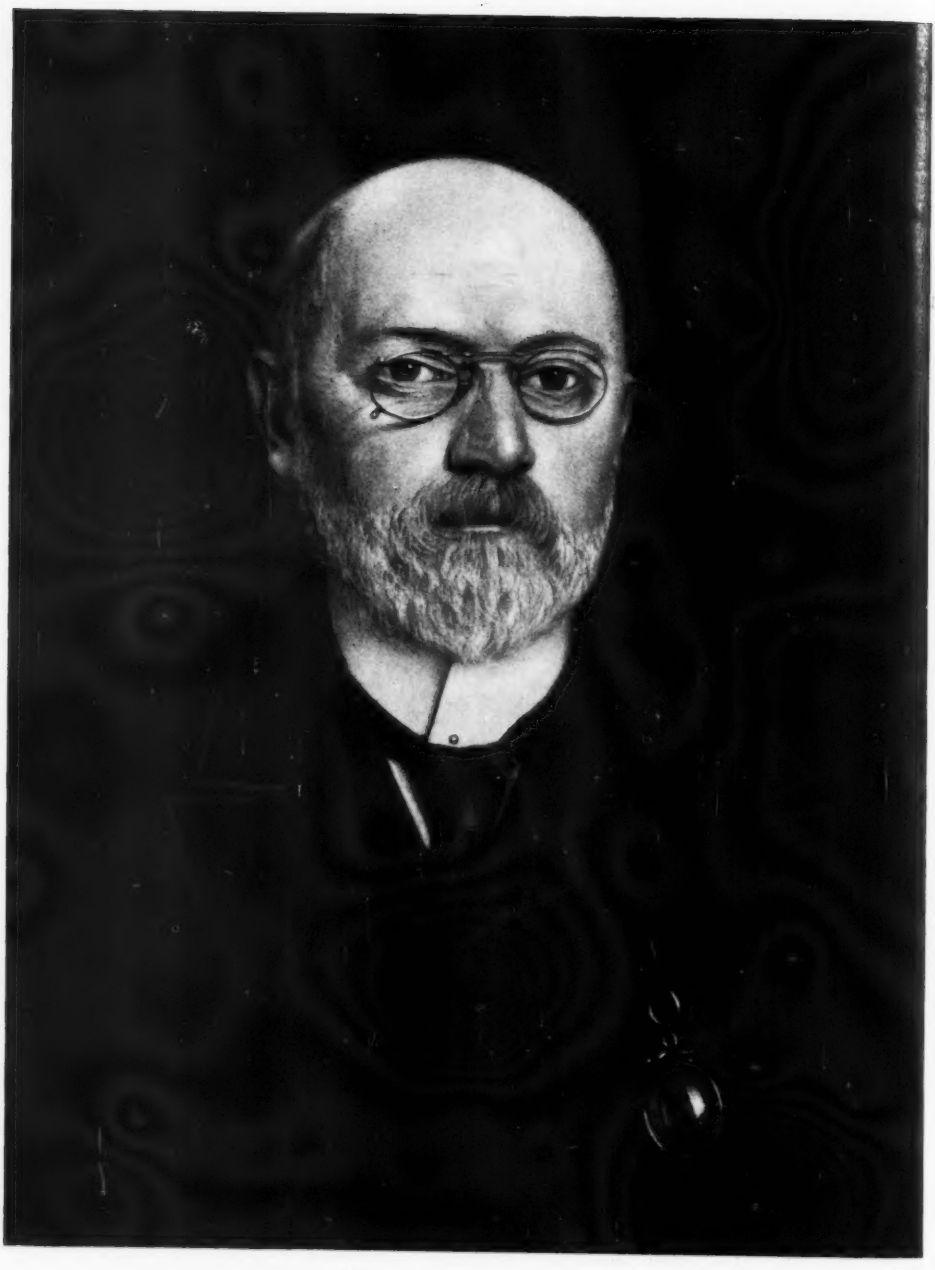
Graham Steell was one of the three original honorary members of the Cardiac Society. He was born in 1851, and died on January 10, 1942, in his ninety-first year. Happily to the very end, he retained to the full all his mental faculties. When, in recent years, the writer visited him in his London home, he often found him engrossed in a text-book of anatomy or medicine and always eager to discuss recent developments and to recall fascinating memories of his own teachers and contemporaries.

Graham Steell was the youngest son of Sir John Steell, sculptor to H.M. Queen Victoria in Scotland. The monument to Sir Walter Scott in Princes Street, which is familiar to all who have visited Edinburgh, was Sir John's work. Educated at the Edinburgh Academy, Steell's early ambition was to be a soldier; but he was persuaded by one of his brothers, for whom he had a great affection, to take up medicine. He qualified at Edinburgh in 1872, and, after spending the following winter studying in Berlin, became house-physician to George Balfour at the Edinburgh Royal Infirmary. It was doubtless this association with Balfour that was responsible for arousing Steell's interest in cardiology and for determining the field of medicine to which he devoted his life's work and in which he was destined to play such a distinguished part.

Except for a few months as resident medical officer to the Stirling Royal Infirmary, the next four years were spent in fever hospitals in Edinburgh, London, and Leeds, and his thesis for the degree of M.D., for which he was awarded a gold medal, was on scarlatina. Prior to coming to Manchester in 1878 he held the appointment of assistant to Professor (afterwards Sir Thomas) Fraser, in the department of materia medica and therapeutics at Edinburgh University.

In 1883, after serving for five years as resident medical officer, Steell was appointed assistant physician to the Manchester Royal Infirmary, to which institution and its patients he gave devoted service until his retirement from the active staff and from the university chair of clinical medicine at the age of sixty.

Amongst his testimonials for this post are many from distinguished men, including William Roberts, Thomas Fraser, William Broadbent, George Balfour, Daniel Leech, Lauder Brunton, Clifford Allbutt, James Ross, F. A. Mahomed, and William Turner. In his testimonial Mahomed wrote, " His modest retiring and courteous disposition must gain the highest esteem of all who have the privilege of knowing him well." The present writer, who had that privilege thirty years later, can find no words that would more aptly describe his character: in fact, his modesty and courtesy would have been almost embarrassing to his younger friends had they not realized the true-hearted kindness that lay below.



In view of his extensive experience in fevers, it is not surprising that many of his early papers were devoted to this subject, but from 1886 onwards, with the exception of occasional excursions into the adjacent pulmonary field, all but two of his publications dealt with cardiology.

His text-book on *Diseases of the Heart*, published in 1906, never achieved the popularity it deserved. In a letter of thanks for a presentation copy, Mackenzie wrote, " Many congratulations on your excellent handbook, and many thanks for the copy. I have been eagerly devouring it, and I have no hesitation in saying it is by far the best book on the heart on the market. Your remarks are so pungent and pithy that it is a delight to read."

This book was no mere compilation of current doctrine: the views expressed were based on the author's own clinical and pathological observations, the full significance of some of which was not apparent until many years later. For example, in reference to œdema he wrote:

> " Capricious distribution of dropsy is specially apt to occur in cases of the cardiac muscle-failure of beer-drinkers and of the disease known as beri-beri, of both of which diseases, it is curious to note, peripheral neuritis is a clinical feature. . . . Curious special localizations of œdema met with, in cases of the kind, have been the scrotum, and together the upper trunk, upper extremities, and scalp and neck, so that the œdema simulates that resulting from mediastinal tumour."

We now know that this type of heart failure, and the peripheral neuritis with which it is often associated, are due to vitamin B_1 deficiency: hence the relation that puzzled Steell, between beri-beri and chronic alcoholism.

Another problem that puzzled him was the occasional association of transient pericardial friction with angina pectoris. His paper recording these observations was published many years before the clinical syndrome of coronary thrombosis was recognized in this country.

The murmur of pulmonary incompetence that bears Steell's name was first described by him in a paper read to the Manchester Medical Society and afterwards published in the *Medical Chronicle* in 1888. He wrote as follows:

> " I wish to plead for the admission among the recognized auscultatory signs of disease of a murmur due to pulmonary regurgitation, such regurgitation occurring independently of disease or deformity of the valves, and as the result of long-continued excess of blood pressure in the pulmonary artery.
>
> " In cases of mitral obstruction there is occasionally heard over the pulmonary area (the sternal extremity of the third left costal cartilage), and below this region for the distance of an inch or two along the left border of the sternum, and rarely over the lowest part of the bone itself, a soft blowing diastolic murmur immediately following, or, more exactly, running off from the accentuated second sound, while the usual indications of aortic regurgitation, afforded by the pulse, etc., are absent. The maximum intensity of the murmur may be regarded as situated at the sternal end of the third and fourth intercostal spaces. When the second sound is reduplicated, the murmur proceeds from its latter part. That such a

murmur as I have described does exist, there can, I think, be no doubt. . . . The murmur of high pressure in the pulmonary artery is not peculiar to mitral stenosis, although it is most commonly met with as a consequence of this lesion. Any long-continued obstruction in the pulmonary circulation may produce it. The pulmonary valves, like the aortic, do not readily become incompetent, apart from structural changes. Probably no amount of blood pressure in the pulmonary artery will render them so suddenly, as, at least theoretically, the mitral valves may be rendered incompetent. Changes in the vessel, with widening of its channel, and, eventually, of its orifice, long precede the occurrence of incompetence of its valves. The pulmonary murmur of high pressure is probably never persistent at first, and one of its most remarkable features is, as a rule, its variableness in intensity. On some days it will be distinctly heard, on others it will be indistinct, or even inaudible; while extreme accentuation of the pulmonary second sound is always present, the closure of the pulmonary semilunar valves being generally perceptible to the hand placed over the pulmonary area, as a sharp thud. This non-persistence of the murmur, in the earlier stages, at any rate, is only what the study of dilatation of the aorta and the consequent regurgitation would lead us to expect. Indeed, so common is a soft blowing murmur, after an accentuated aortic second sound, that extreme accentuation should make us listen, with special care, for a murmur, and even though it be absent on the first occasion the search should not be abandoned. My belief is, that when the aortic second sound is extremely accentuated, regurgitation, to some extent, will probably occur sooner or later. Its supervention in aneurysm of the first part of the arch of the aorta is a familiar fact. Post-mortem, enlargement of the left ventricle, in these cases, may be a better indication of regurgitation having occurred during life than the usual test of filling the cut aorta with water, a proceeding which cannot imitate the action of the forcible blood currents in the living body. An accentuated second sound is no way incompatible with a certain amount of incompetence of the semilunar valves; on the contrary, an accentuated second sound, associated with a regurgitant murmur, is clinically common."

In addition to his text-book and numerous original papers in scientific journals, Steell published three small monographs devoted to the *Physical Signs of Cardiac Disease* (1881), the *Physical Signs of Thoracic Disease* (1900), and *The Use of the Sphygmograph in Clinical Medicine* (1889). The sphygmograph had always fascinated him, and he made a practice of taking pulse tracings from all his cardiac patients. From references to this subject in their correspondence it is evident that these records were of great interest to Mackenzie who, when in practice in Burnley, used often to go round Steell's wards in the Manchester Royal Infirmary. Two men outwardly more different it would be hard to imagine, but they were close friends and had the highest regard for each other's work.

Although keenly interested in auscultation (he always used a monaural stethoscope made of box-wood with a bell-shaped earpiece), Steell laid great

stress on disease of the heart muscle rather than of the valves as the factor of primary clinical importance. His " master," Balfour, had coined the term " curable mitral regurgitation " to distinguish the mitral incompetence associated with conditions such as chlorosis from the " mitral disease " due to a damaged valve. This conception greatly appealed to Steell, and in the preface to his book he wrote:

> " No mitral valves can be competent if they fail to receive that assistance from the heart muscle that they were designed to receive in the performance of their function."

In 1911 Steell delivered the Bradshaw lecture at the Royal College of Physicians. His subject " *Intra-thoracic Tumours and Aneurysms in their Clinical Aspect* " was one that had interested him deeply for many years and afforded ample scope for his special talents. He was at his best as a bedside teacher when demonstrating the physical signs of intrathoracic disease and considering their interpretation.

Steell was a lover of animals, and a staunch advocate of physical exercise: himself a boxer in his youth and later a keen horseman, he often recommended riding as the best form of exercise for those of his cardiac patients whose disability was slight. He was the last Manchester consultant to keep a brougham and pair. In a letter to the writer in 1931, he said, " For the last ten years and more the importance of exercise in the treatment of heart troubles has been more and more borne in upon me and, in my own case, I have more and more made application of it. . . . The beginning of my heart troubles was in 1898: an extreme irregularity and frequency of the pulse, which went on continuously for weeks. I have normally regarded this as auricular fibrillation, but your paper raises doubts in my mind. Your phrase ' showers of extrasystoles ' at any rate appeals to me in a way impossible to anyone who has not gone through experience of such a condition." In addition to heart trouble he had more than his fair share of the diseases he knew so well. In his young days he contracted both typhoid and typhus, and in 1888 he was off work for some months, tubercle bacilli having been found in his sputum.

After the last war Steell retired from practice and went to live with his son, who was for a time in practice in Derbyshire and who later became a medical officer of the Ministry of Health, first in Newcastle and subsequently in London. The writer well remembers the concern of his son, when one day he discovered the old man embarking on an original research on the colour sense of young bullocks by waving a red handkerchief at them in the field adjacent to his house!

He married in 1886 Agnes Dunlop McKie, who was Lady Superintendent of nurses of the Manchester Royal Infirmary. She died in 1910. They had one son, to whom the writer is indebted for the great privilege of having enjoyed the friendship of Graham Steell.

CRIGHTON BRAMWELL.

PRINTED IN GREAT BRITAIN
BY WILLIAM CLOWES AND SONS, LIMITED,
LONDON AND BECCLES.